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(71) Applicant: BRISTOL–MYERS SQUIBB COMPANY [US/US]; P.O. Box 4000, Princeton, NJ 08543–4000 (US).

(72) Inventors: DAS, Jagabandhu; 38 Martin Lane, Mercerville, NJ 08619 (US). BARRISH, Joel, C.; 46 Heather Valley Road, Holland, PA 18966 (US). WITYAK, John; 25 Jared Drive, Robbinsville, NJ 08691 (US).

(74) Agents: SHER, Audrey, F. et al.; Bristol–Myers Squibb Company, P.O. Box 4000, Princeton, NJ 08543–4000 (US).

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(54) Title: BENZOTHIAZOLE PROTEIN TYROSINE KINASE INHIBITORS

(57) Abstract

Novel benzothiazoles and salts thereof, pharmaceutical compositions containing such compounds, and methods of using such compounds in the treatment of protein tyrosine kinase–associated disorders such as immunologic disorders.

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BENZOTHIAZOLE PROTEIN TYROSINE KINASE INHIBITORS

Field of the Invention

The present invention relates to benzothiazoles and salts thereof, to methods of using such compounds in treating protein tyrosine kinase-associated disorders such as immunologic disorders, and to pharmaceutical compositions containing such compounds.

Background of the Invention

Protein tyrosine kinases (PTKs) are enzymes which, in conjuction with ATP as a substrate, phosphorylate tyrosine residues in peptides and proteins. These enzymes are key elements in the regulation of cell signaling including cell proliferation and cell differentiation. PTKs comprise, *inter alia*, receptor tyrosine kinases (RPTKs), including members of the epidermal growth factor kinase family (e.g., HER1 and HER2), platelet derived growth factor (PDGF), and kinases that play a role in angiogenesis (Tie-2 and KDR); and, in addition, non-receptor tyrosine kinases, including members of the Syk, JAK and Src (e.g. src, fyn, lyn, Lck and blk) families (see Bolen, J.B., Rowley, R.B., Spana, C., and Tsygankov, A.Y., "The src family of tyrosine protein kinases in hemopoietic signal transduction", *FASEB J.*, *6*, 3403-3409 (1992); Ullrich, A. and Schlessinger, J., "Signal transduction by receptors with tyrosine kinase activity", *Cell*, *61*, 203-212 (1990); and Ihle, J.N., "The Janus protein tyrosine kinases in hematopoetic cytokine signaling", *Sem. Immunol.*, *7*, 247-254 (1995)).

Enhanced activity of PTKs has been implicated in a variety of malignant and nonmalignant proliferative diseases. In addition, PTKs play a central role in the regulation of cells of the immune system. PTK

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inhibitors can thus impact a wide variety of oncologic and immunologic disorders. Such disorders may be ameliorated by selective inhibition of a certain receptor or non-receptor PTK, such as Lck, or due to the homology among PTK classes, by inhibition of more than one PTK by an inhibitor.

A PTK of particular interest is Lck which is found in T cells where it is involved in phosphorylating key protein substrates. It is required for productive antigen receptor signaling and cell activation. In the absence of Lck activity, the T cell receptor (TCR) zeta chain is not phosphorylated, the kinase ZAP-70 is not activated, and Ca^{2+} mobilization essential for T cell activation does not occur (see Weiss, A. and Littman, D.R., "Signal transduction by lymphocyte antigen receptors", *Cell*, *76*, 263-274 (1994); Iwashima, M., Irving, B.A., van Oers, N.S.C., Chan, A.C., and Weiss, A., "Sequential interactions of the TCR with two distinct cytoplasmic tyrosine kinases", *Science*, *263*, 1136-1139 (1994); and Chan, A.C., Dalton, M., Johnson, R., Kong, G., Wang, T., Thoma, R., and Kurosaki, T., "Activation of ZAP-70 kinase activity by phosphorylation of tyrosine 493 is required for lymphocyte antigen receptor function", *EMBO J.*, *14*, 2499-2508 (1995)). Inhibitors of Lck are thus useful in the treatment of T-cell mediated disorders such as chronic diseases with an important T cell component, for example rheumatoid arthritis, multiple sclerosis and lupus, as well as acute diseases where T cells are known to play an essential role, for example acute transplant rejection and delayed-type hypersensitivity (DTH) reactions.

Summary of the Invention

The present invention provides benzothiazole compounds of the following formula I and salts thereof, for use as protein tyrosine kinase inhibitors:

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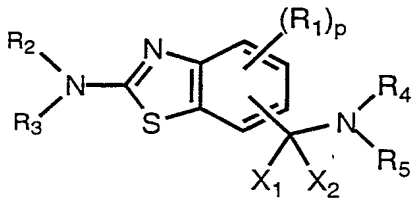

(I)

where

p is 0, 1, 2 or 3;

X_1 and X_2 are each hydrogen, or together form =O or =S;

each R_1 is independently selected from:

(1) hydrogen or R_6,

where R_6 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclo, or heterocycloalkyl, each of which is unsubstituted or substituted with Z_1, Z_2 and one or more (preferably, one or two) groups Z_3;

(2) -OH or -OR_6;

(3) -SH or -SR_6;

(4) -$C(O)_qH$, -$C(O)_qR_6$, or -O-$C(O)_qR_6$, where q is 1 or 2;

(5) -SO_3H or -$S(O)_qR_6$;

(6) halo;

(7) cyano;

(8) nitro;

(9) -Z_4-NR_7R_8;

(10) -Z_4-$N(R_9)$-Z_5-$NR_{10}R_{11}$;

(11) -Z_4-$N(R_{12})$-Z_5-R_6;

(12) -$P(O)(OR_6)_2$;

(13) any two groups R_1 may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the carbon atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(14) any two groups R_1 may, together with the carbons to which they are attached, form a heterocyclo group, which

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group is unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_2 and R_3 are each independently:

(1) hydrogen or R_6;

(2) $-Z_4-R_6$; or

(3) $-Z_{13}-NR_7R_8$;

R_4 and R_5:

(1) are each independently hydrogen or R_6; or

(2) together with the nitrogen atom to which they are attached complete a 3- to 8-membered saturated or unsaturated heterocyclic ring which is unsubstituted or substituted with Z_1, Z_2 and Z_3, which heterocyclic ring may optionally have fused to it a benzene ring itself unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_7, R_8, R_9, R_{10}, R_{11} and R_{12}:

(1) are each independently hydrogen or R_6;

(2) R_7 and R_8 may together be alkylene or alkenylene, completing a 3- to 8-membered saturated or unsaturated ring with the nitrogen atom to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(3) any two of R_9, R_{10} and R_{11} may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_{13} is:

(1) cyano;

(2) nitro;

(3) $-NH_2$;

(4) -NHOalkyl;

(5) -OH;

(6) -NHOaryl;

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(7) -NHCOOalkyl;
(8) -NHCOOaryl;
(9) -$NHSO_2$alkyl;
(10) -$NHSO_2$aryl;
(11) aryl;
(12) heteroaryl;
(13) -Oalkyl; or
(14) -Oaryl;

R_{14} is:

(1) -NO_2;
(2) -COOalkyl; or
(3) -COOaryl;

Z_1, Z_2 and Z_3 are each independently:

(1) hydrogen or Z_6, where Z_6 is (i) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, alkylaryl, cycloalkylaryl, heterocyclo, or heterocycloalkyl; (ii) a group (i) which is itself substituted by one or more of the same or different groups (i); or (iii) a group (i) or (ii) which is substituted by one or more of the following groups (2) to (16) of the definition of Z_1, Z_2 and Z_3;
(2) -OH or -OZ_6;
(3) -SH or -SZ_6;
(4) -$C(O)_qH$, -$C(O)_qZ_6$, or -O-$C(O)_qZ_6$;
(5) -SO_3H or -$S(O)_qZ_6$;
(6) halo;
(7) cyano;
(8) nitro;
(9) -Z_4-NZ_7Z_8;
(10) -Z_4-$N(Z_9)$-Z_5-NZ_7Z_8;
(11) -Z_4-$N(Z_{10})$-Z_5-Z_6;
(12) -Z_4-$N(Z_{10})$-Z_5-H;

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(13) oxo;

(14) -O-C(O)-Z_6;

(15) any two of Z_1, Z_2, and Z_3 may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached; or

(16) any two of Z_1, Z_2, and Z_3 may together be -O-$(CH_2)_q$-O-;

Z_4 and Z_5 are each independently:

(1) a single bond;

(2) -Z_{11}-$S(O)_q$-Z_{12}-;

(3) -Z_{11}-C(O)-Z_{12}-;

(4) -Z_{11}-C(S)-Z_{12}-;

(5) -Z_{11}-O-Z_{12}-;

(6) -Z_{11}-S-Z_{12}-;

(7) -Z_{11}-O-C(O)-Z_{12}-; or

(8) -Z_{11}-C(O)-O-Z_{12}-;

Z_7, Z_8, Z_9 and Z_{10}:

(1) are each independently hydrogen or Z_6;

(2) Z_7 and Z_8, or Z_6 and Z_{10}, may together be alkylene or alkenylene, completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(3) Z_7 or Z_8, together with Z_9, may be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3;

Z_{11} and Z_{12} are each independently:

(1) a single bond;

(2) alkylene;

(3) alkenylene; or

(4) alkynylene;

Z_{13} is:

(1) a single bond;

(2) $-Z_{11}-S(O)_q-Z_{12}-$;

(3) $-Z_{11}-C(O)-Z_{12}-$;

(4) $-Z_{11}-C(S)-Z_{12}-$;

(5) $-Z_{11}-O-Z_{12}-$;

(6) $-Z_{11}-S-Z_{12}-$;

(7) $-Z_{11}-O-C(O)-Z_{12}-$;

(8) $-Z_{11}-C(O)-O-Z_{12}-$;

(9) $-C(NR_{13})-$;

(10) $-C(CHR_{14})-$; or

(11) $-C(C(R_{14})_2)-$.

Detailed Description of the Invention

The following are definitions of terms used in this specification. The initial definition provided for a group or term herein applies to that group or term throughout the present specification, individually or as part of another group, unless otherwise indicated.

The terms "alk" or "alkyl" refer to straight or branched chain hydrocarbon groups having 1 to 12 carbon atoms, preferably 1 to 8 carbon atoms. The expression "lower alkyl" refers to alkyl groups of 1 to 4 carbon atoms.

The term "alkenyl" refers to straight or branched chain hydrocarbon groups of 2 to 10, preferably 2 to 4, carbon atoms having at least one double bond. Where an alkenyl group is bonded to a nitrogen atom, it is preferred that such group not be bonded directly through a carbon bearing a double bond.

The term "alkynyl" refers to straight or branched chain hydrocarbon groups of 2 to 10, preferably 2 to 4, carbon atoms having at least one triple bond. Where an alkynyl group is bonded to a nitrogen atom, it is preferred that such group not be bonded directly through a carbon bearing a triple bond.

The term "alkylene" refers to a straight chain bridge of 1 to 5 carbon atoms connected by single bonds (e.g., $-(CH_2)_x-$ wherein x is 1 to 5), which may be substituted with 1 to 3 lower alkyl groups.

The term "alkenylene" refers to a straight chain bridge of 2 to 5 carbon atoms having one or two double bonds that is connected by single bonds and may be substituted with 1 to 3 lower alkyl groups. Exemplary alkenylene groups are -CH=CH-CH=CH-, $-CH_2-CH=CH-$, $-CH_2-CH=CH-CH_2-$, $-C(CH_3)_2CH=CH-$ and $-CH(C_2H_5)-CH=CH-$.

The term "alkynylene" refers to a straight chain bridge of 2 to 5 carbon atoms that has a triple bond therein, is connected by single bonds, and may be substituted with 1 to 3 lower alkyl groups. Exemplary alkynylene groups are $-C\equiv C-$, $-CH_2-C\equiv C-$, $-CH(CH_3)-C\equiv C-$ and $-C\equiv C-CH(C_2H_5)CH_2-$.

The terms “ar” or "aryl" refer to phenyl, naphthyl and biphenyl.

The terms "cycloalkyl" and "cycloalkenyl" refer to cyclic hydrocarbon groups of 3 to 12 carbon atoms.

The terms "halogen" and "halo" refer to fluorine, chlorine, bromine and iodine.

The term “unsaturated ring” includes partially unsaturated and aromatic rings.

The terms "heterocycle", "heterocyclic" or "heterocyclo" refer to fully saturated or unsaturated, including aromatic (“heteroaryl”) or nonaromatic cyclic groups, for example, 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic ring systems, which have at least one heteroatom in at least one carbon atom-containing ring. Each ring of the heterocyclic group containing a heteroatom may have 1, 2, 3 or 4 heteroatoms selected from nitrogen atoms, oxygen atoms and/or sulfur atoms, where the nitrogen and sulfur heteroatoms may optionally be oxidized and the nitrogen heteroatoms may optionally be quaternized. The heterocyclic group may be attached at any heteroatom or carbon atom of the ring or ring system.

Exemplary monocyclic heterocyclic groups include pyrrolidinyl, pyrrolyl, pyrazolyl, oxetanyl, pyrazolinyl, imidazolyl, imidazolinyl,

imidazolidinyl, oxazolyl, oxazolidinyl, isoxazolinyl, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, 4-piperidonyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, tetrahydropyranyl, morpholinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl, and the like.

Exemplary bicyclic heterocyclic groups include indolyl, benzothiazolyl, benzoxazolyl, benzodioxolyl, benzothienyl, quinuclidinyl, quinolinyl, tetra-hydroisoquinolinyl, isoquinolinyl, benzimidazolyl, benzopyranyl, indolizinyl, benzofuryl, chromonyl, coumarinyl, benzopyranyl, cinnolinyl, quinoxalinyl, indazolyl, pyrrolopyridyl, furopyridinyl (such as furo[2,3-c]pyridinyl, furo[3,2-b]pyridinyl] or furo[2,3-b]pyridinyl), dihydroisoindolyl, dihydroquinazolinyl (such as 3,4-dihydro-4-oxo-quinazolinyl), tetrahydroquinolinyl and the like.

Exemplary tricyclic heterocyclic groups include carbazolyl, benzidolyl, phenanthrolinyl, acridinyl, phenanthridinyl, xanthenyl and the like.

Where q is 1 or 2, "$-C(O)_qH$" denotes -C(O)-H or -C(O)-OH; "$-C(O)_qR_6$" or "$-C(O)_qZ_6$" denote, respectively, $-C(O)-R_6$ or $-C(O)-OR_6$, or $-C(O)-Z_6$ or $-C(O)-OZ_6$; "$-O-C(O)_qR_6$" or "$-O-C(O)_qZ_6$" denote, respectively, $-O-C(O)-R_6$ or $-O-C(O)-OR_6$, or $-O-C(O)-Z_6$ or $-O-C(O)-OZ_6$; and "$-S(O)_qR_6$" or "$-S(O)_qZ_6$" denote, respectively, $-SO-R_6$ or $-SO_2-R_6$, or $-SO-Z_6$ or $-SO_2-Z_6$.

Compounds of the formula I may in some cases form salts which are also within the scope of this invention. Reference to a compound of the formula I herein is understood to include reference to salts thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases. Zwitterions (internal or inner salts) are included within the term "salt(s)" as used herein (and may be formed, for example, where the R substituents comprise an acid moiety such as a carboxyl group). Also included herein are quaternary ammonium salts such as alkylammonium salts. Pharmaceutically acceptable (i.e., non-

toxic, physiologically acceptable) salts are preferred, although other salts are useful, for example, in isolation or purification steps which may be employed during preparation. Salts of the compounds of the formula I may be formed, for example, by reacting a compound I with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

Exemplary acid addition salts include acetates (such as those formed with acetic acid or trihaloacetic acid, for example, trifluoroacetic acid), adipates, alginates, ascorbates, aspartates, benzoates, benzenesulfonates, bisulfates, borates, butyrates, citrates, camphorates, camphorsulfonates, cyclopentanepropionates, digluconates, dodecylsulfates, ethanesulfonates, fumarates, glucoheptanoates, glycerophosphates, hemisulfates, heptanoates, hexanoates, hydrochlorides, hydrobromides, hydroiodides, 2-hydroxyethanesulfonates, lactates, maleates, methanesulfonates, 2-naphthalenesulfonates, nicotinates, nitrates, oxalates, pectinates, persulfates, 3-phenylpropionates, phosphates, picrates, pivalates, propionates, salicylates, succinates, sulfates (such as those formed with sulfuric acid), sulfonates (such as those mentioned herein), tartrates, thiocyanates, toluenesulfonates such as tosylates, undecanoates, and the like.

Exemplary basic salts (formed, for example, where the R substituents comprise an acidic moiety such as a carboxyl group) include ammonium salts, alkali metal salts such as sodium, lithium, and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases (for example, organic amines) such as benzathines, dicyclohexylamines, hydrabamines, N-methyl-D-glucamines, N-methyl-D-glucamides, t-butyl amines, and salts with amino acids such as arginine, lysine and the like. The basic nitrogen-containing groups may be quaternized with agents such as lower alkyl halides (e.g. methyl, ethyl, propyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (e.g. dimethyl, diethyl, dibutyl, and diamyl sulfates), long chain halides (e.g. decyl, lauryl, myristyl and

stearyl chlorides, bromides and iodides), aralkyl halides (e.g. benzyl and phenethyl bromides), and others.

Prodrugs and solvates of the compounds of the invention are also contemplated herein. The term "prodrug", as employed herein, denotes a compound which, upon administration to a subject, undergoes chemical conversion by metabolic or chemical processes to yield a compound of the formula I, or a salt and/or solvate thereof. Solvates of the compounds of formula I are preferably hydrates.

All stereoisomers of the present compounds, such as those which may exist due to asymmetric carbons on the R substituents of the compound of the formula I, including enantiomeric and diastereomeric forms, are contemplated within the scope of this invention. Individual stereoisomers of the compounds of the invention may, for example, be substantially free of other isomers, or may be admixed, for example, as racemates or with all other, or other selected, stereoisomers. The chiral centers of the present invention can have the S or R configuration as defined by the IUPAC 1974 Recommendations.

Throughout the specification, groups and substituents thereof are chosen to provide stable moieties and compounds.

Preferred Compounds

Compounds of the formula I, and salts thereof, wherein one or more, and especially all, of p, X_1, X_2, R_1, R_2, R_3, R_4, and R_5 are selected from the following definitions, are preferred compounds of the present invention:

p is 0 or 1;

each R_1 is independently selected from hydrogen, halo, alkyl or alkoxy;

X_1 and X_2 together form =O or =S;

R_2 is hydrogen;

R_3 is selected from hydrogen, alkyl, $-Z_4-R_6$ or $-Z_{13}-NR_7R_8$;

R_4 is hydrogen; and

R_5 is selected from aryl groups which are substituted with Z_1, Z_2 and one or more (such as one or two) groups Z_3.

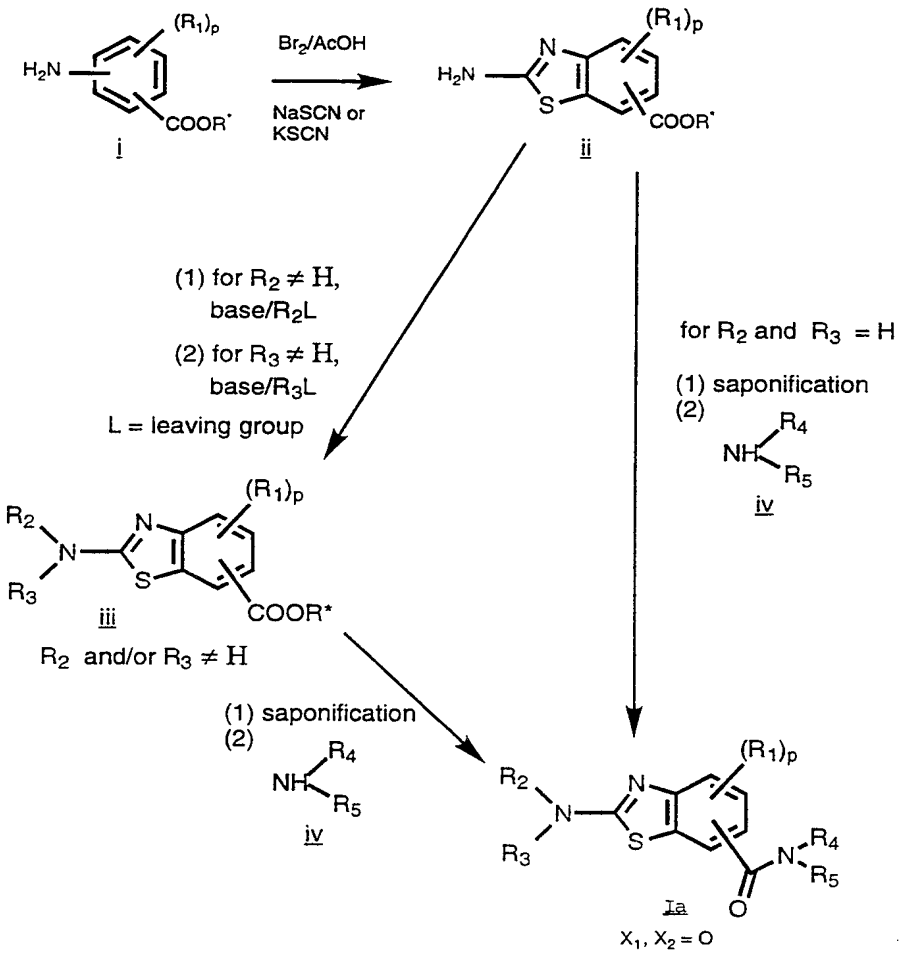
Such compounds where the group $-C(X_1)(X_2)-N(R_4)(R_5)$ of formula I is bonded at the 6-position of the benzothiazole core are particularly preferred.

Methods of Preparation

The compounds of the formula I may be prepared by methods such as those illustrated in the following Schemes A to C and I to X. Solvents, temperatures, pressures, and other reaction conditions may readily be selected by one of ordinary skill in the art. All documents cited are incorporated herein by reference in their entirety. Starting materials are commercially available or readily prepared by one of ordinary skill in the art.

Therefore, one of ordinary skill in the art, upon reading this specification and the documents cited herein, is fully taught how to make the compounds claimed herein.

Scheme A

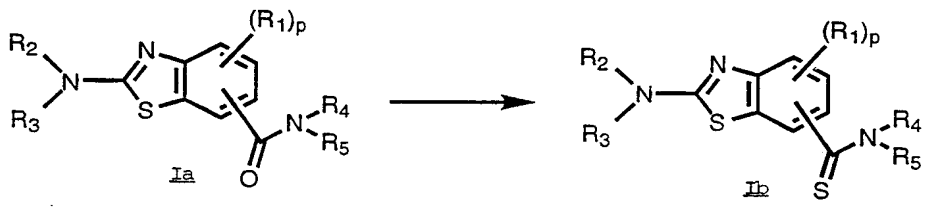

(R1)p
H2N
COOR*
i
Br2/AcOH
NaSCN or
KSCN
ii
(1) for R2 ≠ H,
base/R2L
(2) for R3 ≠ H,
base/R3L
L = leaving group
for R2 and R3 = H
(1) saponification
(2)
R4
NH
R5
iv
R2
N
R3
S
iii
COOR*
R2 and/or R3 ≠ H
(1) saponification
(2)
Ia
X1, X2 = O
O

Scheme A illustrates a general method for forming compound Ia, which is a compound of the formula I where X_1 and X_2 together form =O. As shown in Scheme A, a 2-amino substituted benzothiazolecarboxyate **ii** may be prepared by reacting an appropriately substituted aminobenzoate **i** with sodium or potassium thiocyanate and bromine in an acidic solvent such as acetic acid (see U.S. Patent No. 5,496,816). R* is a carboxyl protecting group such as alkyl or arylalkyl.

Compound Ia where R_2 and R_3 are hydogen may be formed by saponification of **ii** followed by reaction with amine **iv** by methods known in the art. Alternatively, **ii** may be reacted with R_2L where L is a leaving group such as halogen (for example, in equimolar portions), optionally followed by reaction with R_3L (for example, in equimolar portions) to form **iii**. The compound **iii** may then be saponified and reacted with amine **iv** to form Ia where R_2 and/or R_3 are other than hydrogen.

Methods for preparing preferred substituents on the compounds I are illustrated in the following Schemes I to X.

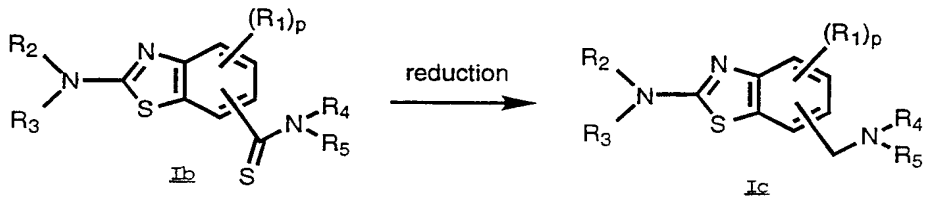
Scheme B



Scheme B illustrates a general method for forming compound Ib, which is a compound of the formula I where X_1 and X_2 together form =S. As shown in Scheme B, the compound of the formula Ia obtained in Scheme A may be converted into the corresponding thioamide Ib using a reagent such as Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (see *Bull. Soc. Chim. Belg.*, *87*, 223 (1978)).

Methods for preparing preferred substituents on the compounds I are illustrated in the following Schemes I to X.

Scheme C

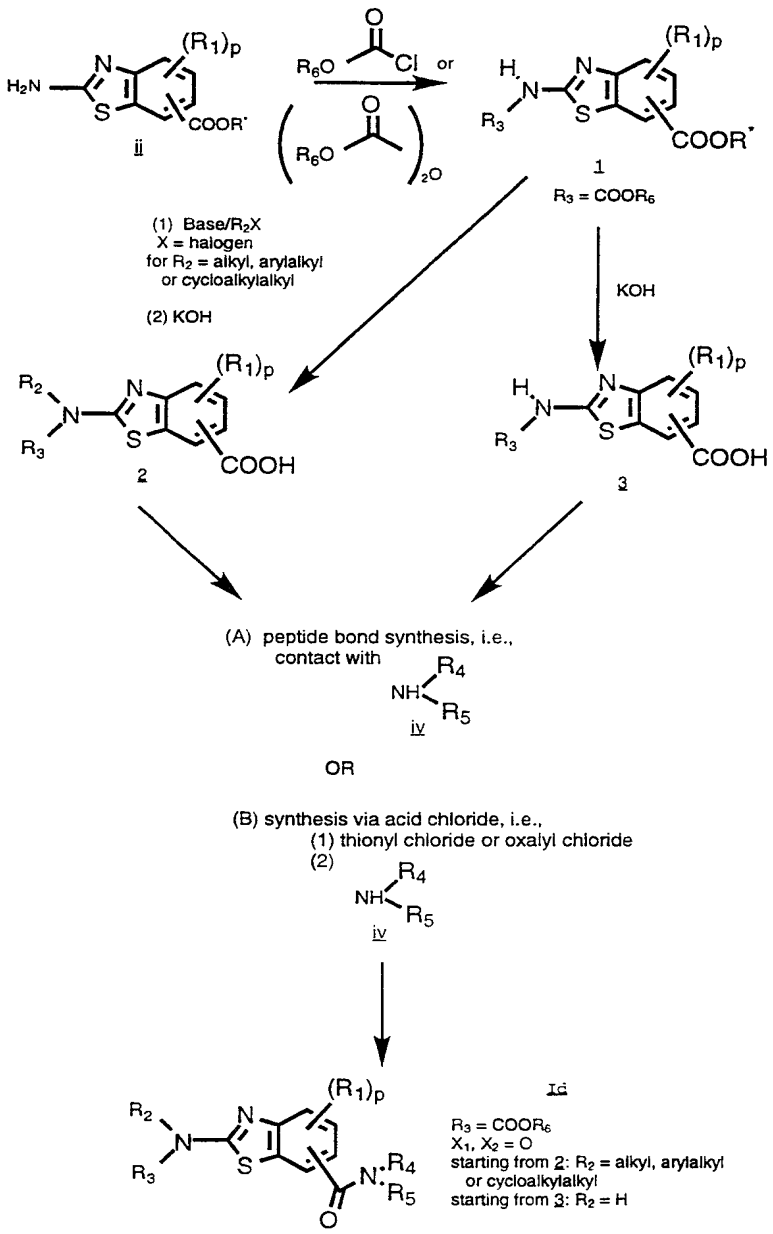


Ib Ic

Scheme C illustrates a general method for forming compound Ic, which is a compound of the formula I where X_1 and X_2 are each hydrogen. As shown in Scheme C, the compound of the formula Ib obtained in Scheme B may be converted into the corresponding amine Ic by reduction, for example, by reaction with Raney nickel.

Methods for preparing preferred substituents on the compounds I are illustrated in the following Schemes I to X.

Scheme I


ii
1
R3 = COOR6
(1) Base/R2X
X = halogen
for R2 = alkyl, arylalkyl
or cycloalkylalkyl
(2) KOH
KOH
2
3
(A) peptide bond synthesis, i.e.,
contact with
iv
OR
(B) synthesis via acid chloride, i.e.,
(1) thionyl chloride or oxalyl chloride
(2)
iv
Id
R3 = COOR6
X1, X2 = O
starting from 2: R2 = alkyl, arylalkyl
or cycloalkylalkyl
starting from 3: R2 = H

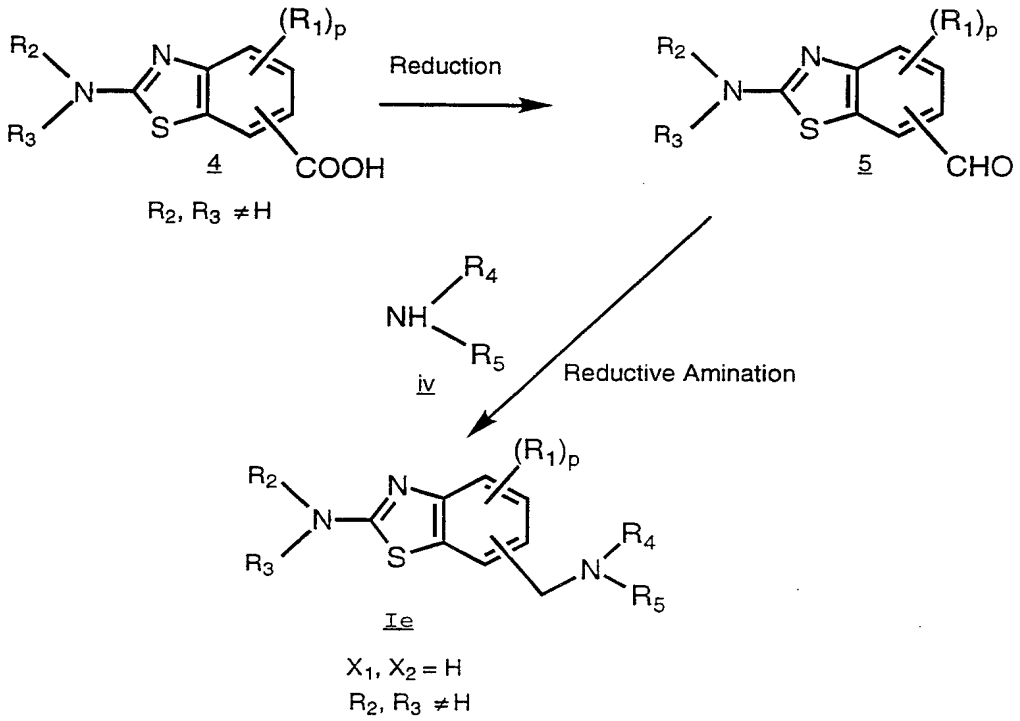
As shown in Scheme I, carboxylate ii can be reacted with a chloroformate or dicarbonate to form 1. Compound 1 can be treated with a base such as sodium hydride, sodium/potassium hexamethyldisilazide, or lithium diisopropylamide (LDA) and an alkylating agent R_2X where X is halogen and R_2 is preferably alkyl, arylalkyl, or cycloalkylalkyl, and then saponified with an aqueous base such as potassium hydroxide to give 2. Compound 1 may, alternatively, be simply saponified with an aqueous base such as potassium hydroxide to give 3 where R_2 is hydrogen.

Acid 2 may be reacted with an amine iv using reaction conditions well known in the art for peptide bond synthesis (see, for example, Bodanszky and Bodanszky, The Practice of Peptide Chemistry, Springer-Verlag, 1984; Bodanszky, Principles of Peptide Synthesis, Springer-Verlag, 1984) to give the compound Id which a compound of the formula I where X_1 and X_2 together form =O, R_3 is $COOR_6$, and, since 2 is the starting material, R_2 is preferably alkyl, arylalkyl or cycloalkylalkyl. For example, reagents which activate the carboxyl group of 2 for reaction with the amine iv include bis-(2-oxo-3-oxazolidinyl)-phosphinic chloride (BOP chloride), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluorophosphate (BOP reagent), [O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium] hexafluorophosphate (HATU), and carbodiimides such as dicyclohexylcarbodiimide (DCC) or 3-ethyl-3'-(dimethylamino)propylcarbodiimide (EDCI) either alone or in combination with a hydroxybenztriazole. Alternatively, the activated ester intermediate can be isolated and then treated with the appropriate amine iv in a nonprotic solvent such as tetrahydrofuran (THF) or dimethylformamide (DMF) in the presence of a base, for example, an organic base such as sodium/potassium hexamethyldisilazide, triethylamine, diisopropylethylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), or an inorganic base such as sodium, potassium or cesium carbonate or sodium or potassium hydride. Alternatively, the acid halide of 2 may be prepared, for example, by reaction with thionyl

chloride or oxalyl chloride, followed by subsequent reaction with amine iv to provide compound Id.

Similar reactions employed above for the conversion of 2 to Id may be used to convert 3 to Id where, in the latter, R_2 is hydrogen.

Scheme II

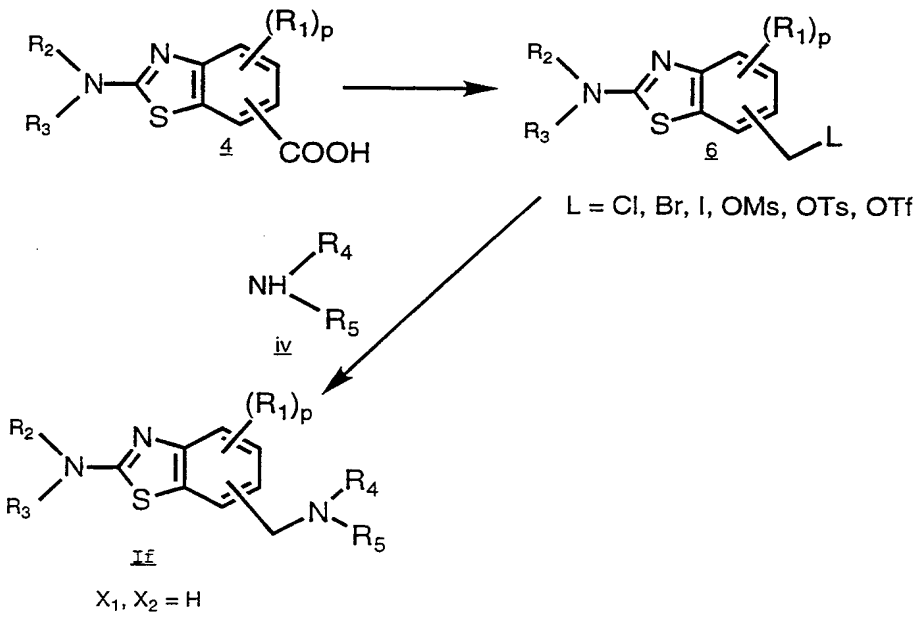


R2, R3 ≠ H

As shown in Scheme II, acid 4 where R_2 and R_3 are not hydrogen and are selected such that the nitrogen to which they are attached is non-basic, is reduced to the aldehyde 5 by methods well know in the art (see March, Advanced Organic Chemistry, Wiley, 1985). For example, the acid 4 may be converted to its corresponding ester followed by reduction with diisobutylaluminum hydride. Alternatively, the acid 4 may be reduced to the corresponding primary alcohol, for example, by treatment with borane/THF, $LiAlH_4$, or via reduction of a mixed anhydride, followed by subsequent oxidation to the aldehyde 5 using Cr(VI) (e.g., pyridinium chlorochromate, "PCC") or under Swern or Moffatt conditions (e.g., $(COCl)_2$/dimethylsulfoxide). The starting acid 4 may be obtained, for example, by saponification of iii.

Reductive amination (see Hudlicky, Reductions in Organic Chemistry, Wiley, 1984) of aldehyde 5 with amine iv in the presence of a reducing agent such as $NaBH_3CN$, $NaBH(OAc)_3$ (Ac = acetyl) or hydrogen and a palladium catalyst produces the amine compound Ie, which is a compound of the formula I where X_1 and X_2 are each hydrogen and R_2 and R_3 are each not hydrogen.

Scheme III

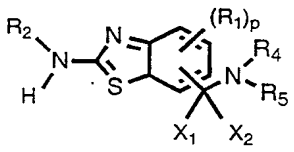


As shown in Scheme III, reduction of the acid **4** to a primary alcohol (for example, by treatment with borane/tetrahydrofuran, $LiAlH_4$, or via reduction of a mixed anhydride), followed by conversion by methods well known in the art (see March, Advanced Organic Chemistry, Wiley, 1985), provides **6** which contains a leaving group such as a halide, tosylate (OTs), mesylate (OMs) or triflate (OTf). The groups R_2 and R_3 are selected such that the resulting nitrogen to which they are attached is non-basic. Compound **6** can then be converted into compound If, which is a compound of the formula I where X_1 and X_2 are each hydrogen, by a displacement reaction with amine **iv**, preferably where amine **iv** is used in excess.

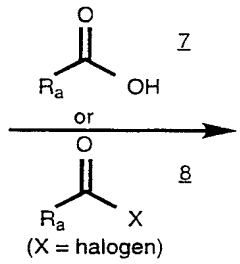
Scheme IV

R_2 = any group as defined
R_3 = acyl or thioacyl

Amide/Thioamide

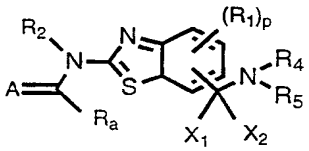


Ia



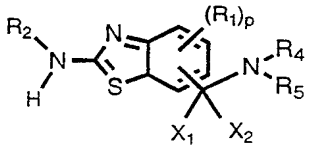
7 or 8

(X = halogen)

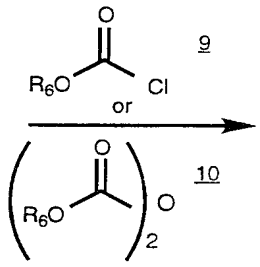


Ih A=O
Ii A=S

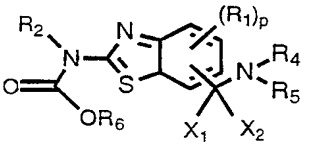
Carbamate



Ia

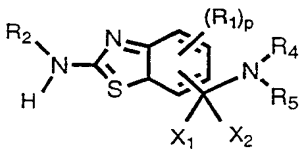


9 or 10



Ij

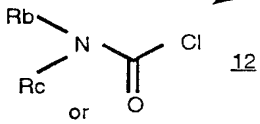
Urea/Thiourea



Ia

1) 9
2) HNR_bR_c 11

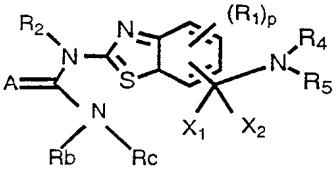
or



12

or

R_bNCO 13a
R_bNCS 13b



Ik A=O
Il A=S

$[X_1, X_2 \neq H]$

Scheme IV illustrates methods which may be used for the preparation of formula I compounds (that is, Ih, Ii, Ij, Ik and Il) where R_2 is any group as defined and R_3 is an acyl or thioacyl group, X_1 and X_2 are not hydrogen, and R_1 is not a primary or secondary amine. The starting compound Ig can be prepared by suitable methods described herein.

Amide Ih can be prepared by treatment of amine compound Ig with a carboxylic acid **7** in the presence of reagents which activate the carboxyl group for reaction as described above, for example BOP reagent, HATU, and carbodiimides such as DCC or EDCI either alone or in combination with a hydroxybenztriazole. Alternatively, the acid halide **8** may be reacted with amine compound Ig in the presence of an acid scavenger such as diisopropylethylamine. The corresponding thioamide Ii can be prepared by the treatment of amide Ih (where $X_1, X_2 \neq O$) with Lawesson's reagent as described above.

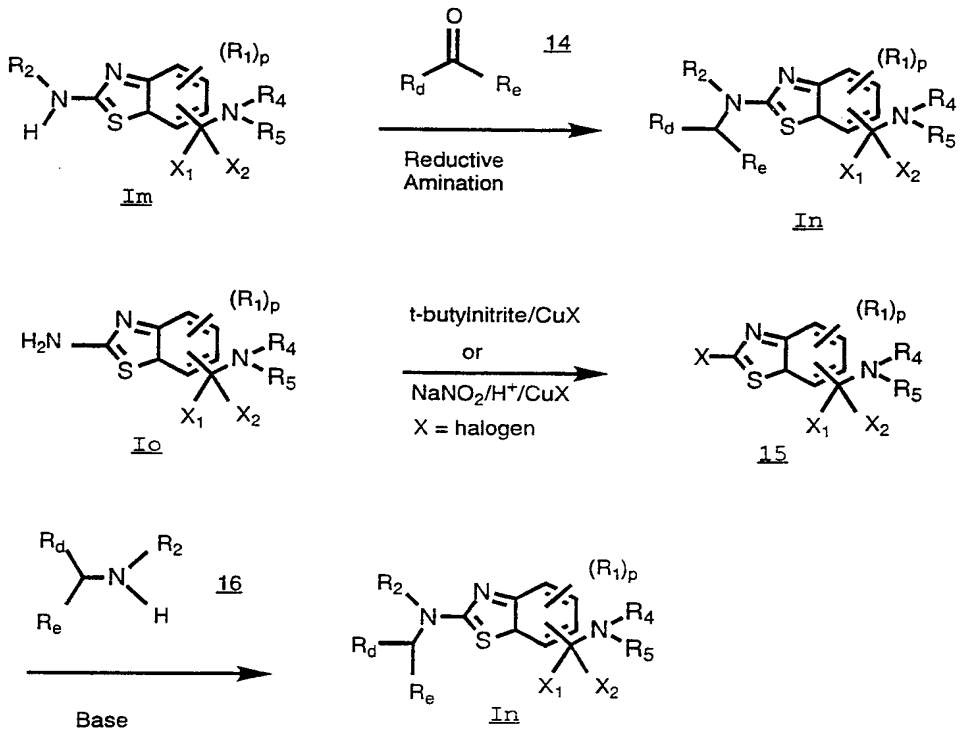
Carbamate Ij can be prepared by treatment of amine compound Ig with a chloroformate **9** or dicarbonate **10** in the presence of an acid scavenger such as diisopropylethylamine.

The urea Ik may be prepared by treatment of amine compound Ig with either: 1) a chloroformate **9**, such as phenylchloroformate, followed by reaction with an amine **11**; 2) a carbamoyl chloride **12** in the presence of an acid scavenger such as diisopropylethylamine; or 3) reaction with an isocyanate **13a** (where R_c in Ik = H). The corresponding thiourea Il may be prepared by treatment of amine compound Ig with a thioisocyanate **13b**.

R_a is selected from those groups included in the definition of R_6 such that the group -C(=A)-R_a is an acyl or thioacyl group within the definition of R_3. R_b and R_c are selected from those groups included in the definitions of R_7 and R_8, such that the group -C(=A)-N(R_b)(R_c) is an acyl or thioacyl group within the definition of R_3.

Scheme V

R_2 = any group as defined other than acyl
R_3 = alkyl, cycloalkyl, cycloalkylalkyl, cycloalkenylalkyl, aralkyl or saturated heterocycle



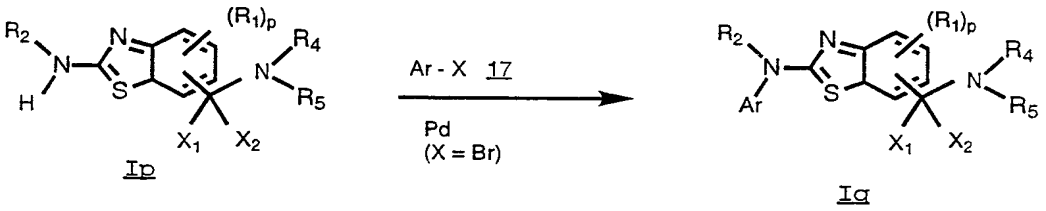
Scheme V illustrates a method which can be used for the preparation of In, which is a compound of the formula I where R_2 is any group as defined other than acyl, and which is selected such that the nitrogen to which it is attached is basic, R_3 is alkyl, cycloalkyl, cycloalkylalkyl, cycloalkenylalkyl, aralkyl, or saturated heterocycle, and X_1 and X_2 together are oxygen. The starting compounds Im and Io can be prepared by suitable methods described herein.

As shown in Scheme V, amine compound Im is reacted with an aldehyde or ketone **14** under reductive amination conditions described above to give the amine In. Compound In may also be prepared by treatment of an amino benzothiazole Io, where R_2 and R_3 are hydrogen, with t-butyl nitrite or sodium nitrite in the presence of a copper (I) halide to give the halo-substituted benzothiazole **15**, followed by displacement with amine **16** in the presence of a base such as sodium or potassium hydride or the like (see Lee et al., *J. Heterocyclic Chemistry, 22*, 1621 (1985)).

R_d and R_e are independently selected from hydrogen, alkyl, aryl, cycloalkyl or cycloalkenyl, or together are alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring, such that the group $-CH(R_d)(R_e)$ is a group within the definition of R_3.

Scheme VI

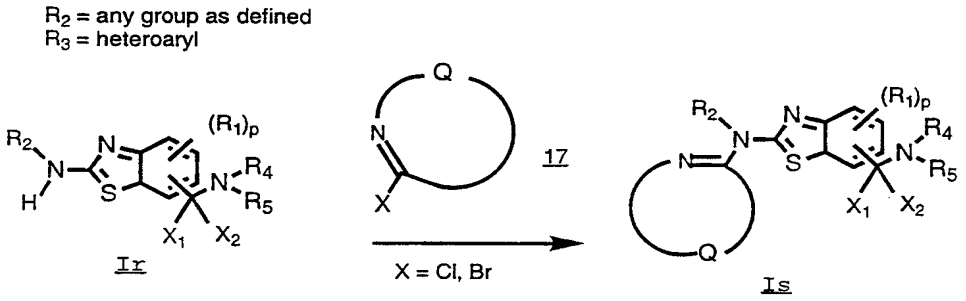
R_2 = any group as defined other than acyl
R_3 = aryl, heteroaryl



Ip Iq

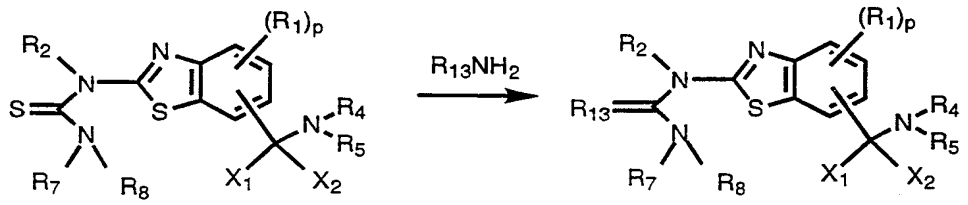
As shown in Scheme VI, when R_2 is any group as defined other than acyl, and is selected such that the nitrogen to which it is attached is basic, R_3 is aryl or heteroaryl, and X_1 and X_2 are not hydrogen, amine compound Ip may be reacted with a halophenyl or haloheteroaromatic group **17** in the presence of a palladium (0) catalyst (see *J. Am. Chem. Soc.*, *118*, 7215 (1996)) to give amine Iq, where Iq is a compound of the formula I having the particular substituents described in this Scheme. The starting compound Ip can be prepared by suitable methods described herein.

Scheme VII



As shown in Scheme VII, when R_2 is any group as defined and R_3 is a heteroaromatic group, amine compound Ir may be reacted with a 2-halosubstituted heteroaromatic compound 17 where Q, together with atoms to which is is bonded, forms a 5- or 6-membered monocyclic or 10- to 12-membered bicyclic heteroaromatic group (such as forming 2-chloropyridine or 2-chloropyrimidine) to give the amine Is, where Is is a compound of the formula I having the particular substituents described in this Scheme. The starting compound Ir can be prepared by suitable methods described herein.

Scheme VIII



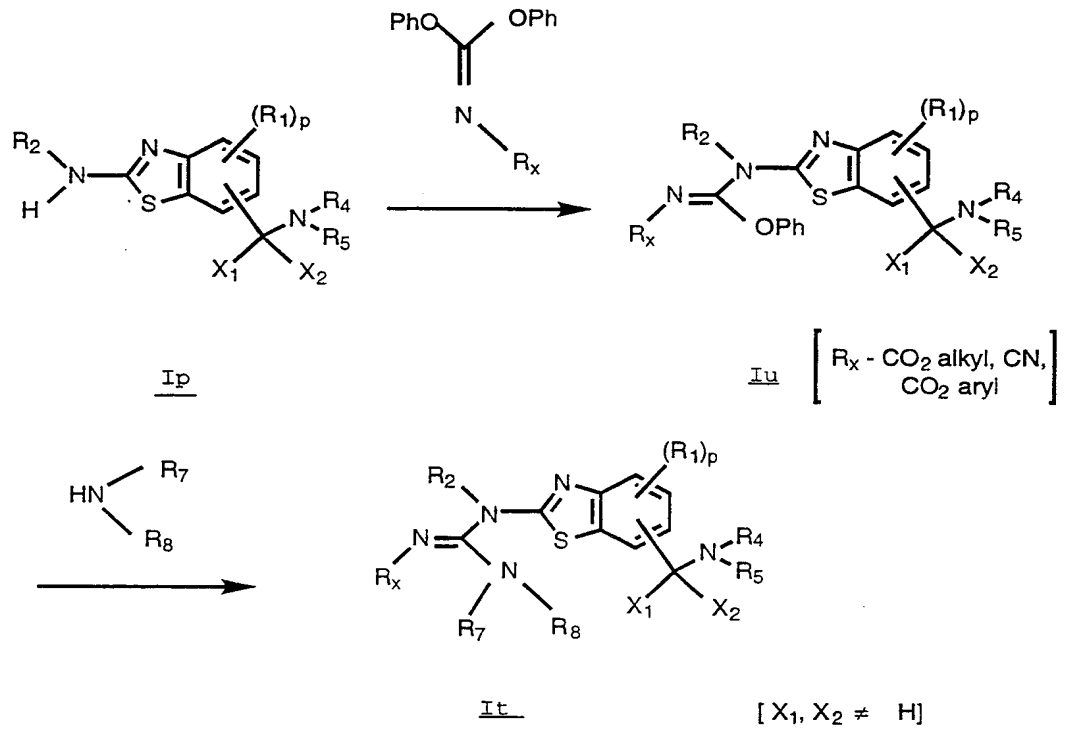
Il It

[$X_1, X_2 \neq$ H]

As shown in Scheme VIII, thiourea compound Il (where X_1 and X_2 are not hydrogen) may be reacted with the appropriate amine in the presence of bis-(2-oxo-3-oxazolidinyl)phosphinic chloride (BOP chloride) benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate (BOP-reagent), [O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium]hexafluorophosphate (HATU) and carbodiimide, such as dicyclohexyl carbodiimide (DCC) or 3-ethyl-3'-(dimethylamino)propyl carbodiimide (EDCI) or diisopropyl carbodiimide (DIC) in the presence of an organic base such as triethylamine, diisopropylethylamine or dimethylaminopyridine in solvents such as dimethylformamide, dichloromethane or tetrahydrofuran to form compound It.

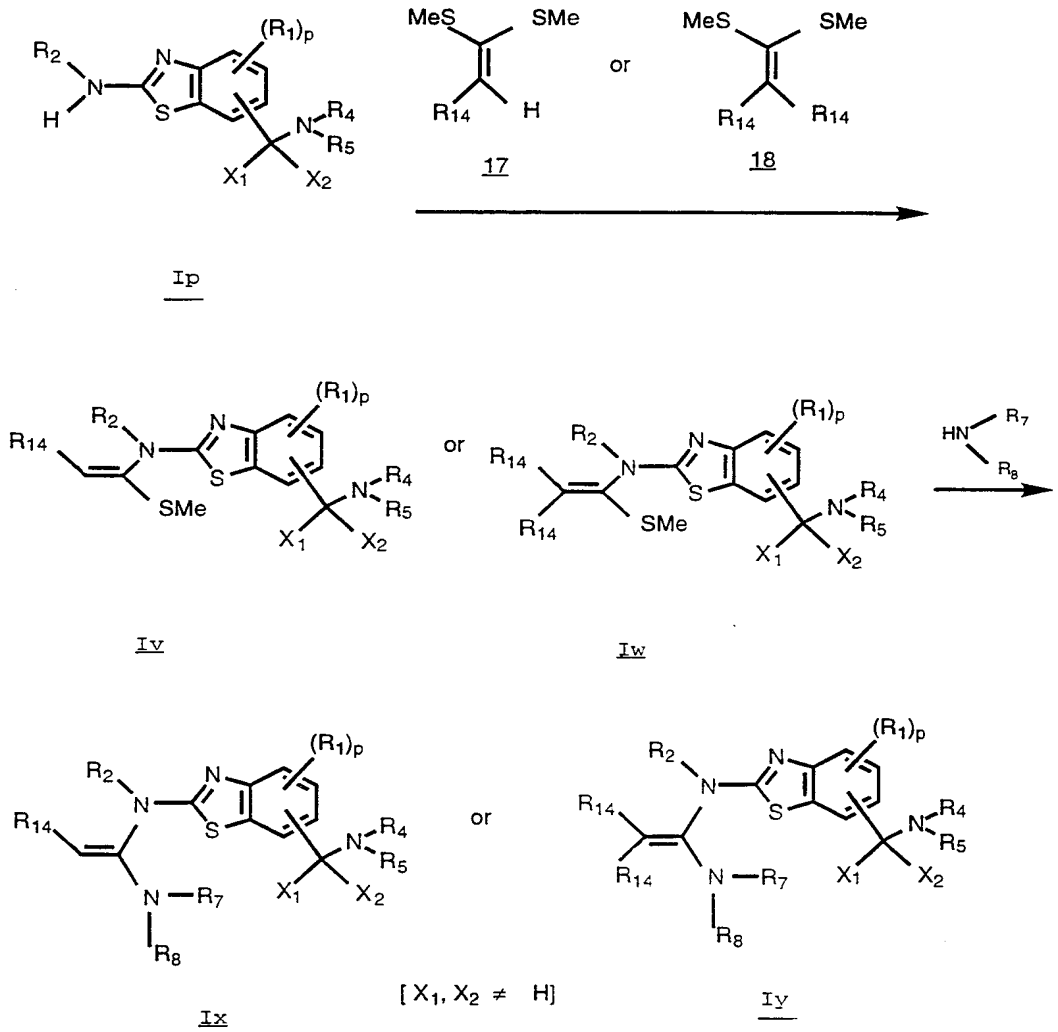
Alternatively, Compound Il can be reacted with the appropriate amine in the presence of a mercury (II) salt such as mercuric chloride to form It, or by other methods known in the literature.

Scheme IX



As shown in Scheme IX, amine Ip (where X_1 and X_2 are not hydrogen) can be reacted with diphenylcyanocarbonimidate either alone or in the presence of a base such as sodium hydride, sodium hexamethyldisilazide or dimethylaminopyridine in acetonitrile or tetrahydrofuran, dimethylformamide at room temperature or elevated temperature to form intermediate compound Iu which can be reacted with an amine (R_7R_8NH) to form compound It (where R=cyanide).

Scheme X



As shown in Scheme X, compound Ip (where X_1 and X_2 are not hydrogen) can be reacted with **17** or **18** either alone or in the presence of a base such as sodium hydride, sodium hexamethyl disilazide or dimethylaminopyridine in dimethyl formamide or tetrahydrofuran at room temperature or higher to form compounds Iv or Iw respectively which can be reacted with an amine (R_7R_8NH) at room temperature or higher to form compounds Ix or Iy respectively.

Utility

The compounds of the present invention inhibit protein tyrosine kinases, especially Lck and, to varying degrees, other Src family kinases such as Fyn, Lyn, Src, Yes, Hck, Fgr and Blk. They are thus useful in the treatment, including prevention and therapy, of protein tyrosine kinase-associated disorders such as immunologic and oncologic disorders. "Protein tyrosine kinase-associated disorders" are those disorders which result from aberrant tyrosine kinase activity, and/or which are alleviated by the inhibition of one or more of these enzymes. For example, Lck inhibitors are of value in the treatment of a number of such disorders (for example, the treatment of autoimmune diseases), as Lck inhibition blocks T cell activation.

Compounds of the present invention inhibit T cell activation. The treatment of T cell mediated diseases, including inhibition of T cell activation and proliferation, is a particularly preferred embodiment of the present invention. Compounds which selectively inhibit T cell activation and proliferation are preferred. Compounds of the present invention which block the activation of endothelial cell PTK by oxidative stress, thereby limiting surface expression of adhesion molecules that induce neutrophil binding, and which inhibit PTK necessary for neutrophil activation are useful, for example, in the treatment of ischemia and reperfusion injury.

The present invention thus provides methods for the treatment of protein tyrosine kinase-associated disorders, comprising the step of administering to a subject in need thereof at least one compound of the formula I in an amount effective therefor. Other therapeutic agents such as those described below may be employed with the inventive compounds in the present methods. In the methods of the present invention, such other therapeutic agent(s) may be administered prior to, simultaneously with or following the administration of the compound(s) of the present invention.

Use of the compounds of the present invention in treating protein tyrosine kinase-associated disorders is exemplified by, but is not limited to, treating a range of disorders such as: transplant (such as organ

transplant, acute transplant or heterograft or homograft (such as is employed in burn treatment)) rejection; protection from ischemic or reperfusion injury such as ischemic or reperfusion injury incurred during organ transplantation, myocardial infarction, stroke or other causes; transplantation tolerance induction; arthritis (such as rheumatoid arthritis, psoriatic arthritis or osteoarthritis); multiple sclerosis; inflammatory bowel disease, including ulcerative colitis and Crohn's disease; lupus (systemic lupus erythematosis); graft vs. host disease; T-cell mediated hypersensitivity diseases, including contact hypersensitivity, delayed-type hypersensitivity, and gluten-sensitive enteropathy (Celiac disease); psoriasis; contact dermatitis (including that due to poison ivy); Hashimoto's thyroiditis; Sjogren's syndrome; Autoimmune Hyperthyroidism, such as Graves' Disease; Addison's disease (autoimmune disease of the adrenal glands); Autoimmune polyglandular disease (also known as autoimmune polyglandular syndrome); autoimmune alopecia; pernicious anemia; vitiligo; autoimmune hypopituatarism; Guillain-Barre syndrome; other autoimmune diseases; cancers where Lck or other Src-family kinases such as Src are activated or overexpressed, such as colon carcinoma and thymoma, or cancers where Src-family kinase activity facilitates tumor growth or survival; glomerulonephritis, serum sickness; uticaria; allergic diseases such as respiratory allergies (asthma, hayfever, allergic rhinitis) or skin allergies; scleracierma; mycosis fungoides; acute inflammatory responses (such as acute respiratory distress syndrome and ishchemia/reperfusion injury); dermatomyositis; alopecia areata; chronic actinic dermatitis; eczema; Behcet's disease; Pustulosis palmoplanteris; Pyoderma gangrenum; Sezary's syndrome; atopic dermatitis; systemic schlerosis; and morphea. The present invention also provides a method for treating the aforementioned disorders such as atopic dermatitis by administration of any compound capable of inhibiting protein tyrosine kinase.

Src-family kinases other than Lck, such as Hck and Fgr, are important in the Fc gamma receptor induced respiratory burst of neutrophils as well as the Fc gamma receptor responses of monocytes

and macrophages. The compounds of the present invention inhibit the Fc gamma induced respiratory burst response in neutrophils. The ability to inhibit Fc gamma receptor dependent responses of neutrophils and potentially other cells' responses could result in additional anti-inflammatory activity for the present compounds beyond their effects on T cells. The activity against T cells and potentially other cells is especially of value, for example, in the treatment of inflammatory diseases such as arthritis or inflammatory bowel disease. In particular, the present compounds are of value for the treatment of autoimmune glomerulonephritis and other instances of glomerulonephritis induced by deposition of immune complexes in the kidney that trigger Fc gamma receptor responses leading to kidney damage.

In addition, Src family kinases other than Lck, such as Lyn and Src, are important in the Fc epsilon receptor induced degranulation of mast cells and basophils that plays an important role in asthma, allergic rhinitis, and other allergic disease. Fc epsilon receptors are stimulated by IgE-antigen complexes. The compounds of the present invention inhibit the Fc epsilon induced degranulation responses, including in the basophil cell line RBL that does not express Lck. The ability to inhibit Fc epsilon receptor dependent mast cell and basophil responses could result in additional anti-inflammatory activity for the present compounds beyond their effect on T cells. The activity of the present compounds towards T cells suggests they could be of value for treatment of asthma, allergic rhinitis, atopic dermatitis and other instances of allergic disease. Activity of the present compounds against mast cells and basophil responses could potentially also be of benefit for treatment of these diseases.

The activity of the present compounds towards T cells is of value in the treatment of any of the aforementioned disorders. Furthermore, the potential combined activity towards T cells , neutrophils and other cells may be of additional value in the treatment of any of the aforementioned disorders.

In a particular embodiment, the compounds of the present invention are useful for the treatment of the aforementioned exemplary

disorders irrespective of their etiology, for example, for the treatment of transplant rejection, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, lupus, graft v. host disease, T-cell mediated hypersensitivity disease, psoriasis, Hashimoto's thyroiditis, Guillain-Barre syndrome, cancer, contact dermatitis, allergic disease such as allergic rhinitis, asthma, ischemic or reperfusion injury, or atopic dermatitis whether or not associated with PTK.

The present invention also provides pharmaceutical compositions comprising at least one of the compounds of the formula I capable of treating a protein tyrosine kinase-associated disorder in an amount effective therefor, and a pharmaceutically acceptable vehicle or diluent. The compositions of the present invention may contain other therapeutic agents as described below, and may be formulated, for example, by employing conventional solid or liquid vehicles or diluents, as well as pharmaceutical additives of a type appropriate to the mode of desired administration (for example, excipients, binders, preservatives, stabilizers, flavors, etc.) according to techniques such as those well known in the art of pharmaceutical formulation.

The compounds of the formula I may be administered by any suitable means, for example, orally, such as in the form of tablets, capsules, granules or powders; sublingually; buccally; parenterally, such as by subcutaneous, intravenous, intramuscular, or intrasternal injection or infusion techniques (e.g., as sterile injectable aqueous or non-aqueous solutions or suspensions); nasally such as by inhalation spray; topically, such as in the form of a cream or ointment; or rectally such as in the form of suppositories; in dosage unit formulations containing non-toxic, pharmaceutically acceptable vehicles or diluents. The present compounds may, for example, be administered in a form suitable for immediate release or extended release. Immediate release or extended release may be achieved by the use of suitable pharmaceutical compositions comprising the present compounds, or, particularly in the case of extended release, by the use of devices such as subcutaneous implants or osmotic pumps. The present compounds may also be administered liposomally.

Exemplary compositions for oral administration include suspensions which may contain, for example, microcrystalline cellulose for imparting bulk, alginic acid or sodium alginate as a suspending agent, methylcellulose as a viscosity enhancer, and sweeteners or flavoring agents such as those known in the art; and immediate release tablets which may contain, for example, microcrystalline cellulose, dicalcium phosphate, starch, magnesium stearate and/or lactose and/or other excipients, binders, extenders, disintegrants, diluents and lubricants such as those known in the art. The present compounds may also be delivered through the oral cavity by sublingual and/or buccal administration. Molded tablets, compressed tablets or freeze-dried tablets are exemplary forms which may be used. Exemplary compositions include those formulating the present compound(s) with fast dissolving diluents such as mannitol, lactose, sucrose and/or cyclodextrins. Also included in such formulations may be high molecular weight excipients such as celluloses (avicel) or polyethylene glycols (PEG). Such formulations may also include an excipient to aid mucosal adhesion such as hydroxy propyl cellulose (HPC), hydroxy propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (SCMC), maleic anhydride copolymer (e.g., Gantrez), and agents to control release such as polyacrylic copolymer (e.g., Carbopol 934). Lubricants, glidants, flavors, coloring agents and stabilizers may also be added for ease of fabrication and use.

Exemplary compositions for nasal aerosol or inhalation administration include solutions in saline which may contain, for example, benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, and/or other solubilizing or dispersing agents such as those known in the art.

Exemplary compositions for parenteral administration include injectable solutions or suspensions which may contain, for example, suitable non-toxic, parenterally acceptable diluents or solvents, such as mannitol, 1,3-butanediol, water, Ringer's solution, an isotonic sodium chloride solution, or other suitable dispersing or wetting and

suspending agents, including synthetic mono- or diglycerides, and fatty acids, including oleic acid.

Exemplary compositions for rectal administration include suppositories which may contain, for example, a suitable non-irritating excipient, such as cocoa butter, synthetic glyceride esters or polyethylene glycols, which are solid at ordinary temperatures, but liquify and/or dissolve in the rectal cavity to release the drug.

Exemplary compositions for topical administration include a topical carrier such as Plastibase (mineral oil gelled with polyethylene).

The effective amount of a compound of the present invention may be determined by one of ordinary skill in the art, and includes exemplary dosage amounts for an adult human of from about 0.1 to 100 mg/kg of body weight of active compound per day, which may be administered in a single dose or in the form of individual divided doses, such as from 1 to 4 times per day. It will be understood that the specific dose level and frequency of dosage for any particular subject may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the species, age, body weight, general health, sex and diet of the subject, the mode and time of administration, rate of excretion, drug combination, and severity of the particular condition. Preferred subjects for treatment include animals, most preferably mammalian species such as humans, and domestic animals such as dogs, cats and the like, subject to protein tyrosine kinase-associated disorders.

The compounds of the present invention may be employed alone or in combination with each other and/or other suitable therapeutic agents useful in the treatment of protein tyrosine kinase-associated disorders such as PTK inhibitors other than those of the present invention, antiinflammatories, antiproliferatives, chemotherapeutic agents, and immunosuppressants.

Exemplary such other therapeutic agents include the following: cyclosporins (e.g., cyclosporin A), CTLA4-Ig, antibodies such as anti-ICAM-3, anti-IL-2 receptor (Anti-Tac), anti-CD45RB, anti-CD2, anti-CD3

(OKT-3), anti-CD4, anti-CD80, anti-CD86, monoclonal antibody OKT3, agents blocking the interaction between CD40 and gp39, such as antibodies specific for CD40 and/or gp39 (i.e., CD154), fusion proteins constructed from CD40 and gp39 (CD40Ig and CD8gp39), inhibitors, such as nuclear translocation inhibitors, of NF-kappa B function, such as deoxyspergualin (DSG), non-steroidal antiinflammatory drugs (NSAIDs) such as ibuprofen, steroids such as prednisone or dexamethasone, gold compounds, antiproliferative agents such as methotrexate, FK506 (tacrolimus, Prograf), mycophenolate mofetil, cytotoxic drugs such as azathiprine and cyclophosphamide, TNF-α inhibitors such as tenidap, anti-TNF antibodies or soluble TNF receptor, and rapamycin (sirolimus or Rapamune) or derivatives thereof, and the PTK inhibitors disclosed in the following U.S. Patent Applications, incorporated herein by reference in their entirety: Serial No. 09/097,338 , filed June 15, 1998, and Serial No. 09/094,797 filed June 15, 1998. See the following documents and references cited therein: Hollenbaugh, D., Douthwright, J., McDonald, V., and Aruffo, A., "Cleavable CD40Ig fusion proteins and the binding to sgp39", *J. Immunol. Methods* (Netherlands), *188(1)*, p. 1-7 (Dec 15 1995); Hollenbaugh, D., Grosmaire, L.S., Kullas, C.D., Chalupny, N.J., Braesch-Andersen, S., Noelle, R.J., Stamenkovic, I., Ledbetter, J.A., and Aruffo, A., "The human T cell antigen gp39, a member of the TNF gene family, is a ligand for the CD40 receptor: expression of a soluble form of gp39 with B cell co-stimulatory activity", *EMBO J* (England), *11(12)*, p 4313-4321 (Dec 1992); and Moreland, L.W. et al., "Treatment of rheumatoid arthritis with a recombinant human tumor necrosis factor receptor (p75)-Fc fusion protein, *New England J. of Medicine, 337(3)*, p. 141-147 (1997).

The above other therapeutic agents, when employed in combination with the compounds of the present invention, may be used, for example, in those amounts indicated in the Physicians' Desk Reference (PDR) or as otherwise determined by one of ordinary skill in the art.

The following assays can be employed in ascertaining the degree of activity of a compound ("test compound") as a PTK inhibitor.

Compounds described in the following Examples have been tested in one or more of these assays, and have shown activity.

Enzyme Assay Using Lck, Fyn, Lyn, Hck, Fgr or Src

The following assay has been carried out using the protein tyrosine kinases *Lck, Fyn, Lyn, Hck, Fgr* and *Src*.

The protein tyrosine kinase of interest is incubated in kinase buffer (20 mM MOPS, pH7, 10 mM $MgCl_2$) in the presence of the test compound. The reaction is initiated by the addition of substrates to the final concentration of 1 μM ATP, 3.3 μCi/ml [33P] gamma-ATP, and 0.1 mg/ml acid denatured enolase (prepared as described in Cooper, J.A., Esch, F.S., Taylor, S.S., and Hunter, T., "Phosphorylation sites in enolase and lactate dehydrogenase utilized by tyrosine protein kinases in vivo and in vitro", *J. Biol. Chem.*, *259*, 7835-7841 (1984)). The reaction is stopped after 10 minutes by the addition of 10% trichloroacetic acid, 100 mM sodium pyrophosphate followed by 2 mg/ml bovine serum albumin. The labeled enolase protein substrate is precipitated at 4 degrees, harvested onto Packard Unifilter plates and counted in a Topcount scintillation counter to ascertain the protein tyrosine kinase inhibitory activity of the test compound (activity inversely proportional to the amount of labeled enolase protein obtained). The exact concentration of reagents and the amount of label can be varied as needed.

This assay is advantageous as it employs an exogenous substrate (enolase) for more accurate enzyme kinetics, and can be conducted in a 96-well format that is readily automated. In addition, His-tagged protein tyrosine kinases (described below) offer much higher production yields and purity relative to GST-protein tyrosine kinase fusion protein.

The protein tyrosine kinase may be obtained from commercial sources or by recombinant methods described herewith. For the preparation of recombinant Lck, human Lck was prepared as a His-tagged fusion protein using the Life Technologies (Gibco) baculovirus vector pFastBac Hta (commercially available) in insect cells. A cDNA encoding human Lck isolated by PCR (polymerase chain reaction) was inserted into the vector and the protein was expressed using the methods

described by the manufacturer. The Lck was purified by affinity chromatography. For the production of Lck in insect cells using baculovirus, see Spana, C., O'Rourke, E.C., Bolen, J.B., and Fargnoli, J., "Analysis of the tyrosine kinase p56lck expressed as a glutathione S-transferase protein in *Spodoptera frugiperda* cells," *Protein expression and purification*, Vol. 4, p. 390-397 (1993). Similar methods may be used for the recombinant production of other Src-family kinases.

Cell assays

(1) Cellular tyrosine phosphorylation

Jurkat T cells are incubated with the test compound and then stimulated by the addition of antibody to CD3 (monoclonal antibody G19-4). Cells are lysed after 4 minutes or at another desired time by the addition of a lysis buffer containing NP-40 detergent. Phosphorylation of proteins is detected by anti-phosphotyrosine immunoblotting. Detection of phosphorylation of specific proteins of interest such as ZAP-70 is detected by immunoprecipitation with anti-ZAP-70 antibody followed by anti-phosphotyrosine immunoblotting. Such procedures are described in Schieven, G.L., Mittler, R.S., Nadler, S.G., Kirihara, J.M., Bolen, J.B., Kanner, S.B., and Ledbetter, J.A., "ZAP-70 tyrosine kinase, CD45 and T cell receptor involvement in UV and H_2O_2 induced T cell signal transduction", *J. Biol. Chem.*, *269*, 20718-20726 (1994), and the references incorporated therein. The Lck inhibitors inhibit the tyrosine phosphorylation of cellular proteins induced by anti-CD3 antibodies.

For the preparation of G19-4, see Hansen, J.A., Martin, P.J., Beatty, P.G., Clark, E.A., and Ledbetter, J.A., "Human T lymphocyte cell surface molecules defined by the workshop monoclonal antibodies," in *Leukocyte Typing I*, A. Bernard, J. Boumsell, J. Dausett, C. Milstein, and S. Schlossman, eds. (New York: Springer Verlag), p. 195-212 (1984); and Ledbetter, J.A., June, C.H., Rabinovitch, P.S., Grossman, A., Tsu, T.T., and Imboden, J.B., "Signal transduction through CD4 receptors: stimulatory vs. inhibitory activity is regulated by CD4 proximity to the CD3/T cell receptor", *Eur. J. Immunol.*, *18*, 525 (1988).

(2) Calcium assay

Lck inhibitors block calcium mobilization in T cells stimulated with anti-CD3 antibodies. Cells are loaded with the calcium indicator dye indo-1, treated with anti-CD3 antibody such as the monoclonal antibody G19-4, and calcium mobilization is measured using flow cytometry by recording changes in the blue/violet indo-1 ratio as described in Schieven, G.L., Mittler, R.S., Nadler, S.G., Kirihara, J.M., Bolen, J.B., Kanner, S.B., and Ledbetter, J.A., "ZAP-70 tyrosine kinase, CD45 and T cell receptor involvement in UV and H_2O_2 induced T cell signal transduction", *J. Biol. Chem.*, *269*, 20718-20726 (1994), and the references incorporated therein.

(3) Proliferation assays

Lck inhibitors inhibit the proliferation of normal human peripheral blood T cells stimulated to grow with anti-CD3 plus anti-CD28 antibodies. A 96 well plate is coated with a monoclonal antibody to CD3 (such as G19-4), the antibody is allowed to bind, and then the plate is washed. The antibody bound to the plate serves to stimulate the cells. Normal human peripheral blood T cells are added to the wells along with test compound plus anti-CD28 antibody to provide co-stimulation. After a desired period of time (e.g., 3 days), the [3H]-thymidine is added to the cells, and after further incubation to allow incorporation of the label into newly synthesized DNA, the cells are harvested and counted in a scintillation counter to measure cell proliferation.

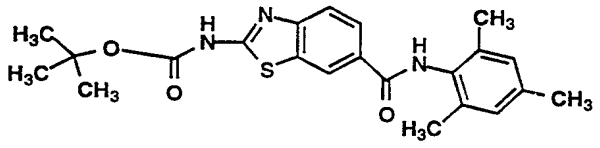
The following Examples illustrate embodiments of the present invention, and are not intended to limit the scope of the claims. Abbreviations employed in the Examples are defined below. Compounds of the Examples are identified by the example and step in which they are prepared (for example, "1A" denotes the title compound of step A of Example 1), or by the example only where the compound is the title compound of the example (for example, "2" denotes the title compound of Example 2).

Abbreviations

aq. = aqueous
conc. = concentrated
DMSO = dimethylsulfoxide
EtOAc = ethyl acetate
Et_2O = diethyl ether
h = hours
HATU = N-[dimethylamino-1H-1,2,3-triazolo-[4,5-b]pyridin-1-yl methylene]-N-methyl methanaminium hexafluorophosphate N-oxide
MeOH = methanol
MOPS = 4-morpholine-propanesulfonic acid
MS = mass spectrometry
Ret Time = retention time
RT = room temperature
satd. = saturated
TFA = trifluoroacetic acid
THF = tetrahydrofuran

Example 1

Preparation of [6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



A. Ethyl-2-amino-benzothiazole-6-carboxylate

A solution of ethyl-4-aminobenzoate (35 g, 212 mmol) in glacial acetic acid (300 mL) was added to a stirred solution of sodium thiocyanate (69 g, 848 mmol) in acetic acid (150 mL). The mixture was cooled in an ice-water bath and a solution of bromine (12 mL, 233 mmol) in acetic acid (60 mL) was added dropwise via an addition funnel. The reaction mixture was stirred at 0°C to RT for 4 h and then poured into water (1.5 L). Saturated sodium carbonate solution was added to neutralize the solution. Precipated solid was filtered, washed with water and EtOAc, and dried *in vacuo* to obtain the title compound of this step (31.65 g, 67.2% yield).

B. Ethyl-2-tert-butoxycarbonyloxyamino-benzothiazole-6-carboxylate

A suspension of **1A** (10 g, 45 mmol), di-t-butyldicarbonate (11.78 g, 54 mmol) and 4-dimethylaminopyridine (549 mg, 4.5 mmol) in dichloromethane (330 mL) was stirred at RT overnight. Additional di-t-butyldicarbonate (3 g, 13.75 mmol) was added. After 20 h, the mixture was concentrated under reduced pressure and the residue was diluted with a 1:1 mixture of EtOAc and Et_2O (200 mL). Solid was filtered and dried *in vacuo* to obtain the title compound of this step (10.5 g, 72.4% yield).

C. 2-tert-Butoxycarbonyloxyamino-benzothiazole-6-carboxylic acid

A 1 N solution of sodium hydroxide in water (931 mL) was added to a suspension of **1B** (10 g, 31.05 mmol) in methanol (170 mL). The mixture was stirred at RT overnight, cooled to 0°C and acidified with aqueous HCl solution. The precipitated solid was filtered, washed with water and dried under reduced pressure. The solid was suspended in tetrahydrofuran and concentrated under reduced pressure. It was further diluted with toluene and concentrated under reduced pressure to remove water. The solid was collected and dried *in vacuo* over phosphorus pentoxide to obtain the title acid of this step (8.32 g, 91% yield).

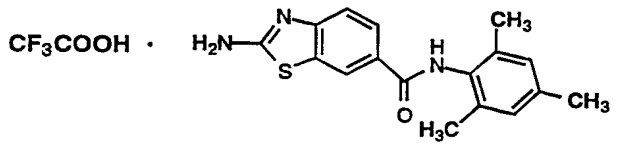
D. [6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

Diisopropylethyl amine (1.83 mL, 10.48 mmol) was added to a stirred suspension of **1C** (2.57 g, 8.73 mmol), 2,4,6-trimethylaniline (1.47 mL, 10.48 mmol) and HATU (3.98 g, 10.48 mmol) in dimethylformamide (77.1 mL). The solution was stirred at RT overnight and then diluted with EtOAc (70 mL). The reaction mixture was washed with 2 N aq. HCl solution (80 mL). The aq. layer was extracted with EtOAc (25 mL). The EtOAc extracts were combined, washed with 2 N aq. HCl solution (60 mL), brine, dried (Na_2SO_4), and concentrated. The crude residue was triturated with a 4:1 mixture of ether and EtOAc (100 mL). Solid was collected and dried *in vacuo* to obtain the title compound of this Example (2.88 g, 80.1% yield).

MS = 412.2 (M^+ + H)

Example 2

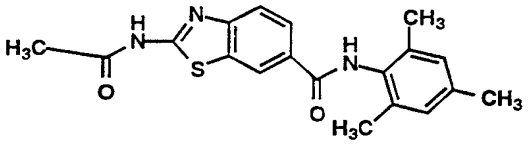
Preparation of 2-Amino-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1)



A solution of **1D** (77.8 mg, 0.19 mmol) in trifluoroacetic acid (5.3 mL) was stirred at RT for 1.5 h. The solution was concentrated under reduced pressure and the residue was coevaporated with ether. Trituration with ether-hexanes mixture gave the title product (62 mg, 72% yield) as an off-white solid.
MS = 311.9 (M^+ + H)

Example 3

Preparation of 2-(Acetylamino)-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



A. Ethyl-2-acetamido-benzothiazole-6-carboxylate

A suspension of **1A** (150 mg, 0.67 mmol) and acetic anhydride (0.18 mL, 1.86 mmol) in dichloromethane (19 mL) and pyridine (3.7 mL) was stirred at RT. After 2 h, additional pyridine (3 mL) and 4-dimethylaminopyridine (8.2 mg, 0.067 mmol) were added. The mixture was stirred for 16 h, diluted with dichloromethane (20 mL) and washed with 2 N aq. HCl solution (20 mL, 3x), saturated. aq. $KHCO_3$ solution (20 mL, 2x) and brine. The dichloromethane extract was dried (Na_2SO_4), filtered and concentrated. The residue was triturated with an ether - hexanes mixture to obtain the title compound of this step (130 mg, 73% yield).

B. 2-Acetamido-benzothiazole-6-carboxylic acid

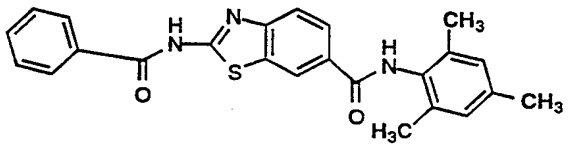
A 2 M aq. solution of potassium hydroxide (5.7 mL) and ethanol (8 mL) were added to a a solution of **3A** (100 mg, 0.38 mmol) in THF (5 mL). The homogenous solution was stirred at RT overnight, cooled to 0°C and acidified with 6 M aq. HCl solution. Most of the ethanol and THF were removed by distillation under reduced pressure. The precipitated solid was filtered, washed with water and dried *in vacuo* to obtain the title acid of this step (64 mg, 72% yield) as a white solid.

C. 2-(Acetylamino)-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

Analogous to the preparation of **1D** except using **3B** to give the title compound of this Example as a light yellow solid (21.5%).
MS = 354 (M^+ + H)

Example 4

Preparation of 2-(Benzoylamino)-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



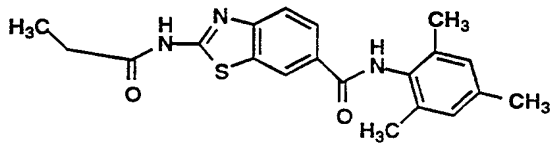
A solution of the free base of **2** (100 mg, 0.32 mmol, obtained by treatment of a solution of the trifluoroacetate salt **2** in dichloromethane with aq. sodium bicarbonate solution) and benzoic anhydride (200 mg, 0.89 mmol) in THF (8.9 mL) and pyridine (1.8 mL) was stirred at RT overnight. Additional benzoic anhydride (200 mg, 0.89 mmol) and 4-dimethylaminopyridine (3.9 mg, 0.032 mmol) were added and the solution was stirred for 2 days. Additional 4-dimethylaminopyridine (3.9 mg, 0.032 mmol) was added and the solution was stirred for an additional 1 h. The mixture was diluted with dichloromethane (40 mL), washed with 1 N aq. HCl solution (15 mL), dried (Na_2SO_4), filtered and concentrated. The residue was triturated with ether to obtain a white

solid which was suspended in dichloromethane and washed with saturated. aq. $KHCO_3$ solution (3x). The dichloromethane extract was dried (Na_2SO_4), filtered and concentrated. Trituration of the crude solid with EtOAc (15 mL) afforded the title compound (49 mg, 37%) as a white solid.

MS = 416.1 (M^+ + H)

Example 5

Preparation of 2-[(1-Oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

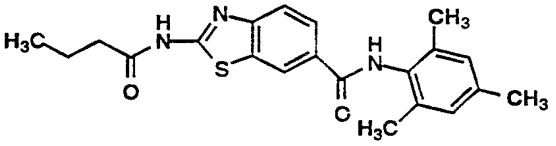


Analogous to the preparation of 4 except using propionic anhydride gave the title compound **5** as a white solid.

MS = 367 (M^+ + H)

Example 6

Preparation of 2-[(1-Oxobutyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

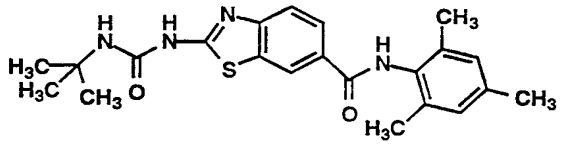


Analogous to the preparation of 4 except using butyric anhydride gave the title compound **6** as a white solid.

MS = 382 (M^+ + H)

Example 7

Preparation of 2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



A. 2-[[[Phenoxy]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

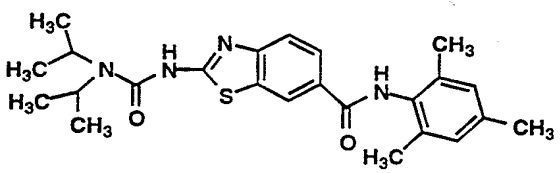
Phenyl chloroformate (470 mg, 3 mmol) was added dropwise to a stirred solution of the free base of **2** (311 mg, 1 mmol) in THF (20 mL) and saturated. aq. $KHCO_3$ solution (20 mL) at 0-5°C. The biphasic mixture was stirred for 3 h. The THF layer was separated and the aqueous layer was extracted with dichloromethane (30 mL, 2x). The organic extracts were combined, dried ($MgSO_4$), filtered and concentrated. The crude residue was diluted with EtOAc (25 mL) and the solid was filtered, washed with EtOAc (8 mL, 4x), and dried *in vacuo* to obtain the title compound of this step as a white solid (269 mg, 62%).

B. 2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

tert-Butyl amine (73 mg, 1 mmol) was added to a stirred solution of **7A** (22 mg, 0.05 mmol) in THF (5 mL). The solution was stirred at RT for 16 h, diluted with dichloromethane (30 mL) and washed with 2 N aq. HCl solution (10 mL, 2x) and 0.5 N aq. NaOH solution (10 mL, 2x). The dichloromethane extract was dried ($MgSO_4$), filtered and concentrated to obtain the title compound of this Example (17 mg, 80%) as a white solid. MS = 411.1 (M^+ + H)

Example 8

Preparation of 2-[[[Bis(1-methylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

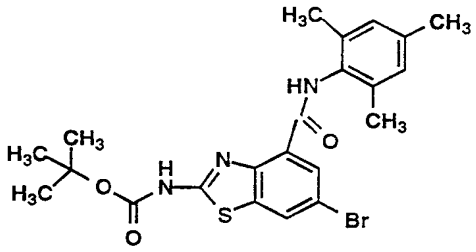


Analogous to the preparation of **7B** except using diisopropyl amine to give the title compound **8** as an off-white solid (78.5%).

MS = 439.2 (M^+ + H)

Example 9

Preparation of [6-Bromo-4-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

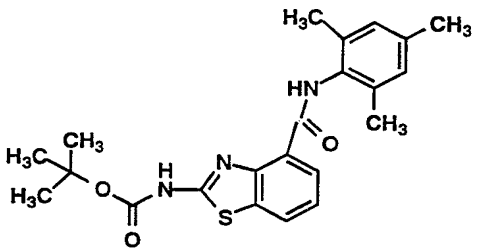


Analogous to the preparation of **1** except using methyl-2-amino-6-bromo-benzothiazole-4-carboxylate (U.S. Patent No. 5,496,816) in place of **1A** to give the title compound **9** as a white solid.

MS = 491.8 (M^+ + H)

Example 10

Preparation of [4-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

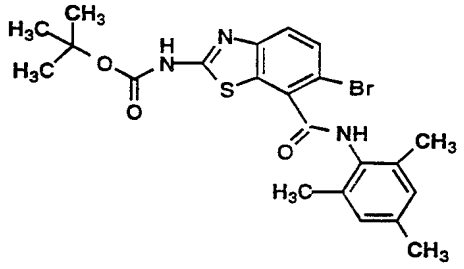


Palladium hydroxide (40 mg) was added to a stirred suspension of **9** (50 mg, 0.1 mmol) in absolute ethanol (60 mL). The reaction flask was equipped with a hydrogen filled balloon via a three way stopcock. Air inside the flask was evacuated under reduced pressure and then filled with hydrogen from the balloon. This operation was repeated (3x). Hydrogenolysis was continued overnight. The reaction mixture was filtered through a pad of anhydrous $MgSO_4$. Residual solid was washed with ethanol (10 mL, 3x). The filtrate was concentrated and the crude residue was chromatographed on a silica gel column. Elution with 5% EtOAc in hexanes, followed by 10% and 20% EtOAc in hexanes afforded the title compound **10** (37 mg, 88%) as a white solid.

MS = 412.1 (M^+ + H)

Example 11

Preparation of [6-Bromo-7-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



A. Methyl-3-amino-6-bromo-benzoate

Tin (II) chloride dihydrate (22.56 g, 100 mmol) was added to a stirred solution of methyl-2-bromo-5-nitrobenzoate (9 g, 34.61 mmol) in

methanol (250 mL) and conc. HCl (25 mL). The solution was stirred at RT for 8 h and then treated with satd. aq. $KHCO_3$ solution (600 mL). Additional solid $KHCO_3$ (50 g) was added. The mixture was extracted with EtOAc (200 mL, 5x). The EtOAc extracts were combined, dried ($MgSO_4$), filtered and concentrated. The residue was diluted with EtOAc (250 mL) and washed with brine (50 mL, 2x), dried ($MgSO_4$), filtered and concentrated to obtain the title compound of this step (7.45 g, 94%) as a brown oil.

B. Methyl-2-amino-6-bromo-benzothiazole-7-carboxylate (**11Ba**) and Methyl-2-amino-6-bromo-benzothiazole-5-carboxylate (**11Bb**)

Analogous to the preparation of **1A** except using **9A** in place of ethyl-4-aminobenzoate as the starting aniline. Trituration of the crude residue with EtOAc afforded pure **11Ba** (43%). The filtrate was concentrated and the residue was chromatographed on a silica gel column. Elution with 10% EtOAc in hexanes, followed by 20%, 30%, and 50% EtOAc in hexanes gave a 1:1 mixture of **11Ba** and **11Bb** (13%) as a yellow solid.

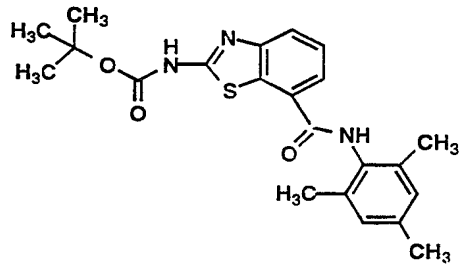
C. [6-Bromo-7-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

Analogous to the preparation of **1D** except using **11Ba** in place of **1A** afforded the title compound as a white solid.

MS = 491.9 (M^+ + H)

Example 12

Preparation of [7-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

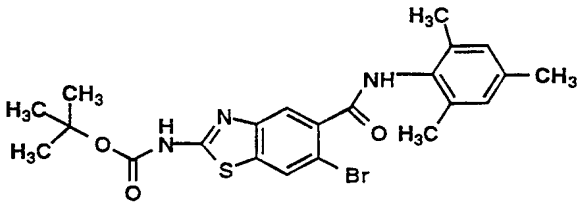


Analogous to the preparation of **10** except using **11C** in place of **9** gave the title compound **12** (89%) as a white solid.

MS = 412.1 (M^+ + H)

Example 13

Preparation of [6-Bromo-5-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

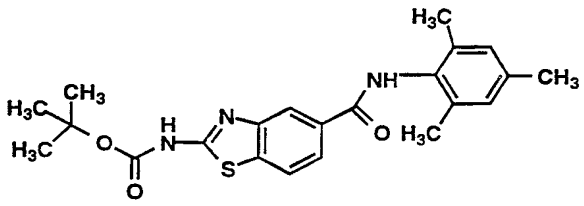


Analogous to the preparation of **1D** except using a 1:1 mixture of **11Ba** and **11Bb** as the starting benzothiazole in place of **1A**. The crude product obtained after work up was diluted with EtOAc and let stand at RT for 2 h. The precipitated solid was filtered, washed with EtOAc, and dried *in vacuo* to obtain the title compound **13** as a white solid.

MS = 492.0 (M^+ + H)

Example 14

Preparation of [5-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

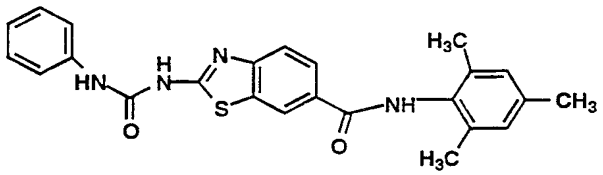


Analogous to the preparation of **10** except using **13** in place of **9** gave the title compound **14** (63%) as a white solid.

MS = 412.1 (M^+ + H)

Example 15

Preparation of 2-[[[Phenylamino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

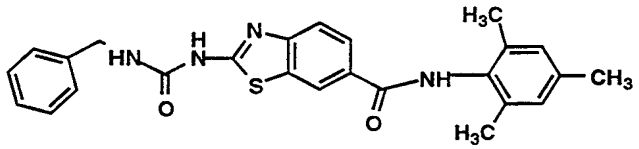


A solution of the free base of **2** (100 mg, 0.32 mmol), phenyl isocyanate (119 mg, 1 mmol) and 4-dimethylaminopyridine (10 mg) in THF (2 mL) and pyridine (2 mL) was stirred at RT overnight. The mixture was diluted with dichloromethane (30 mL) and washed with 2 N aq. HCl solution (20 mL, 2x). The dichloromethane extract was diluted with methanol (10 mL), dried ($MgSO_4$), filtered and concentrated. The crude residue was diluted with EtOAc (25 mL) and the solid was filtered, and washed with EtOAc (5 mL, 3x). The white solid was suspended in dichloromethane (30 mL) and methanol (2 mL) and stirred for 20 min, and filtered. Residual solid was washed with dichloromethane (5 mL, 3x), and dried *in vacuo* to obtain the title compound **15** (88 mg, 64%).

MS = 431.1 (M^+ + H)

Example 16

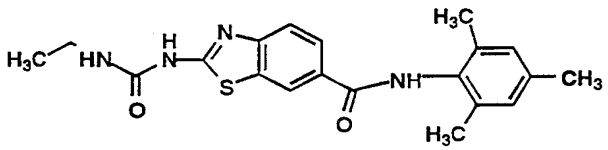
Preparation of 2-[[[(Phenylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **15** except using benzyl isocyanate gave the title compound **16** as a white solid.
MS = 445 (M^+ + H)

Example 17

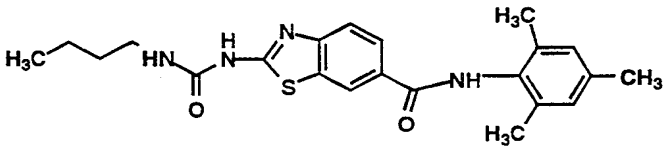
Preparation of 2-[[[Ethylamino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **15** except using ethyl isocyanate gave the title compound **17** as a white solid.
MS = 383 (M^+ + H)

Example 18

Preparation of 2-[[(Butylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **15** except using n-butyl isocyanate gave the title compound **18** as a white solid.
MS = 411 (M^+ + H)

Examples 19 to 58

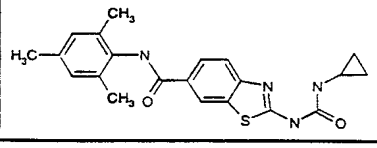
General Procedure

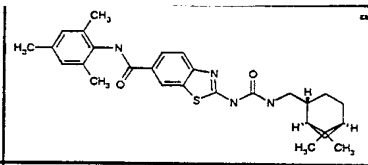
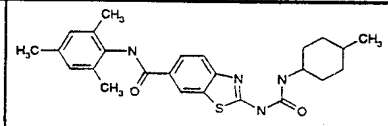
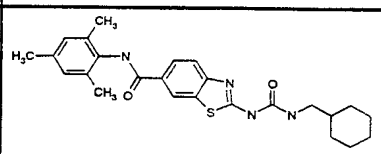
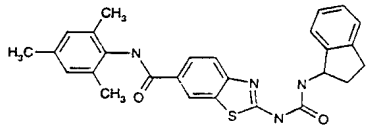
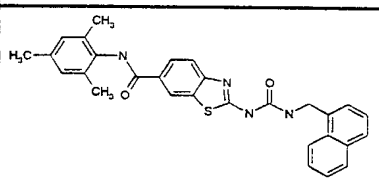
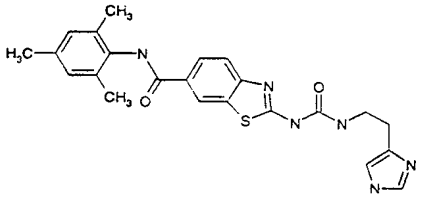
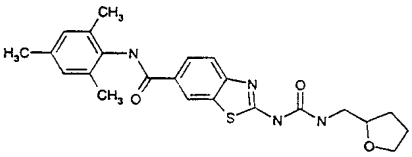
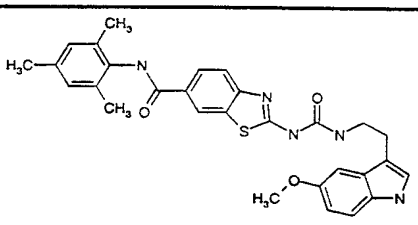
Compounds **19** to **58** were prepared following the procedure described below.

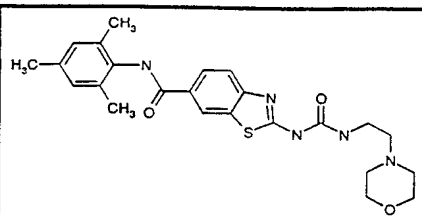
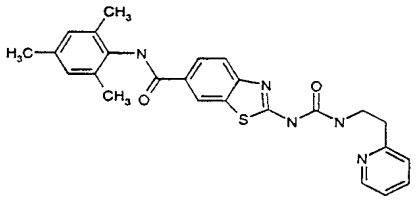
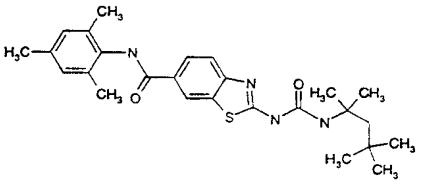
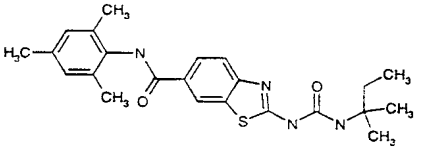
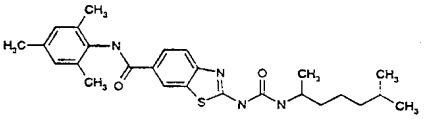
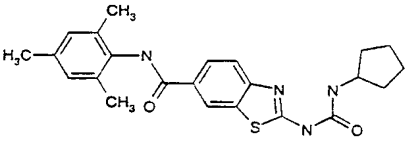
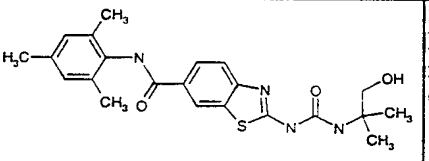
The appropriate amine (0.08 mmol) was added to a solution of **7A** (20 mg, 0.054 mmol) in THF (3 mL). The solution was stirred at RT for 18 to 40 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (1.5 mL, 2x), and 1 N aq. NaOH solution (1.5 mL, 2x). The organic extract was dried ($MgSO_4$), filtered and concentrated *in vacuo* to obtain the compounds of these Examples, identified in Table 1 below.

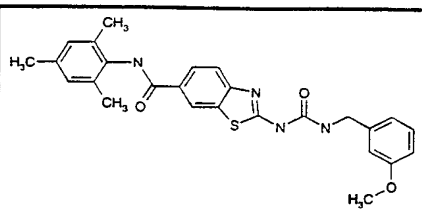
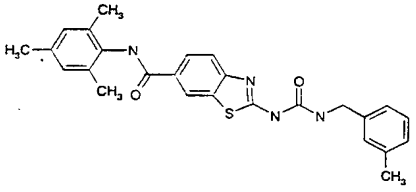
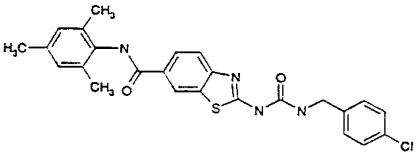
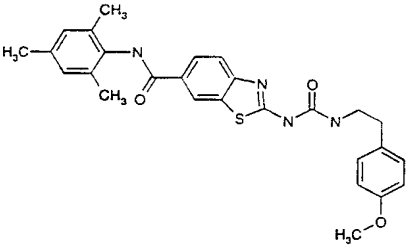
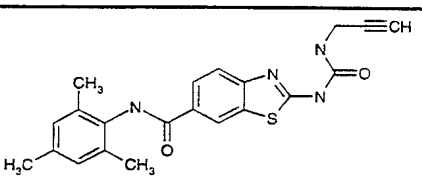
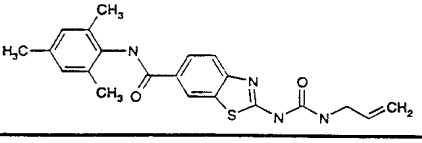
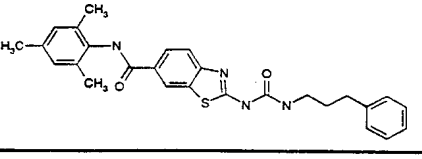
In Table 1, "HPLC Ret Time" was the HPLC retention time obtained under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 4 mL/min, λ = 220 nM for compounds **19** to **56**. For compounds **57** to **58**, HPLC conditions were: Zorbax SB-C18 4.5 mm x 7.5 cm short column, 8 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 2.5 mL/min, λ = 217 nM.

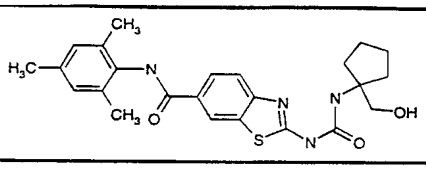
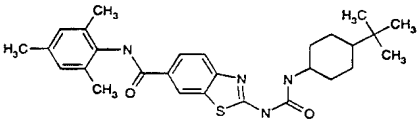
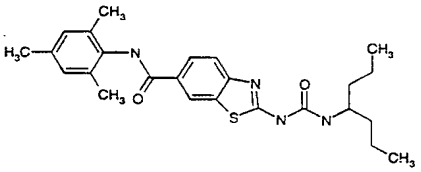
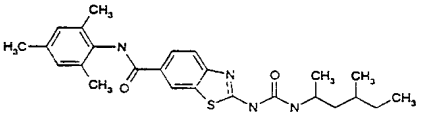
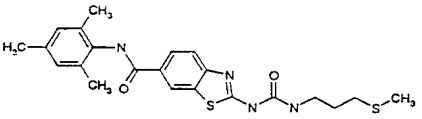
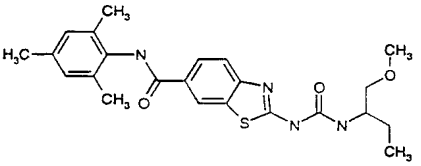
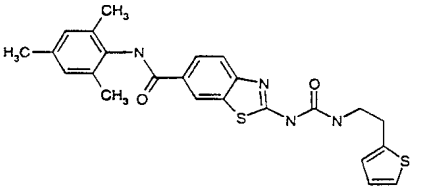
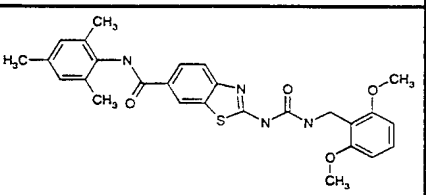
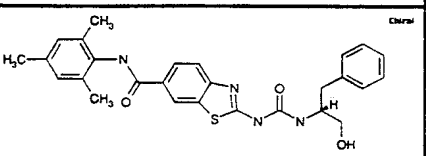
TABLE 1

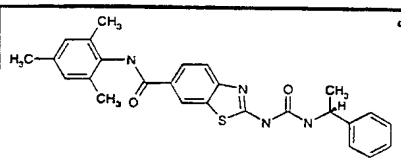
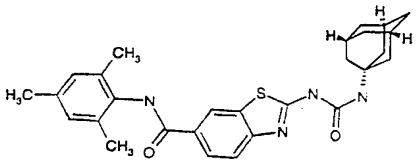
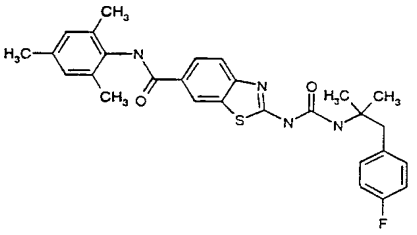
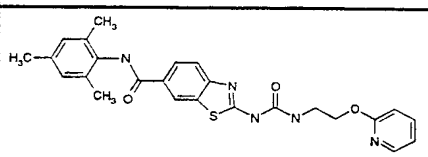
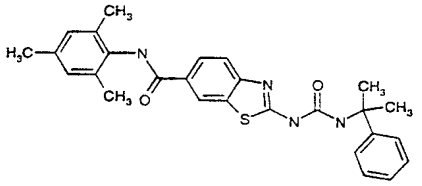
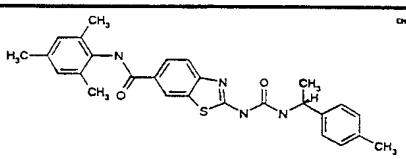
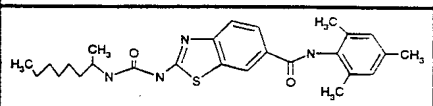
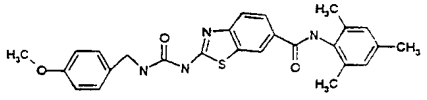
Ex. No.	Compound Structure	Compound Name	HPLC Ret Time (min)
19		2-[[(Cyclopropylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.88

20		(R)-2-[[[[(3,3-Dimethylcyclohexyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.81
21		2-[[[(4-Methylcyclohexyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.52
22		2-[[[(Cyclohexylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.53
23		2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.40
24		2-[[[(1-Naphthalenylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.53
25		2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.19
26		2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.14
27		2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.19

28		2-[[[[2-(4-Morpholinyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.08
29		2-[[[[2-(2-Pyridinyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.17
30		2-[[[(1,1,3,3-Tetramethylbutyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.64
31		2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.32
32		2-[[[(1,5-Dimethylhexyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.74
33		2-[[(Cyclopentylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.28
34		2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.90

35		2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.19
36		2-[[[[(3-Methylphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.34
37		2-[[[[(4-Chlorophenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.37
38		2-[[[[2-(4-Methoxyphenyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.30
39		2-[[(2-Propynylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.66
40		2-[[(2-Propenylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.94
41		2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.45

42		2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.07
43		2-[[[[4-(1,1-Dimethylethyl)cyclohexyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.87
44		2-[[[(1-Propylbutyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.54
45		2-[[[(1,3-Dimethylpentyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.57
46		2-[[[[3-(Methylthio)propyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.08
47		2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.05
48		2-[[[[2-(2-Thienyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.24
49		2-[[[[(2,6-Dimethoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.31
50		(R)-2-[[[[1-(Hydroxymethyl)-2-phenylethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.13

51		(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.28
52		2-[[(1-Adamantylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.74
53		2-[[[[2-(4-Fluorophenyl)-1,1-dimethylethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.54
54		2-[[[[2-(2-Pyridinyloxy)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.97
55		2-[[[(1-Methyl-1-phenylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.36
56		(R)-2-[[[[1-(4-Methylphenyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.44
57		2-[[[(1-Methylheptyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	9.75
58		2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	8.38

Examples 59 to 95

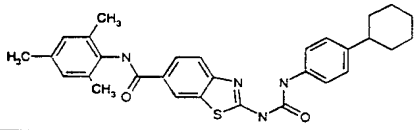
General Procedure

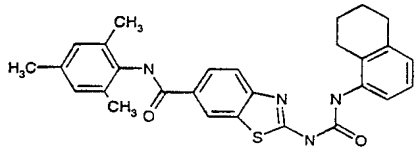
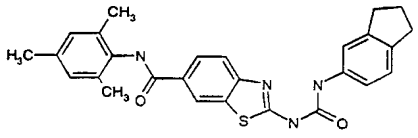
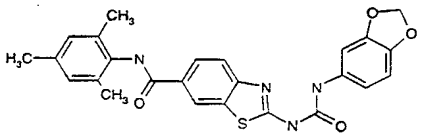
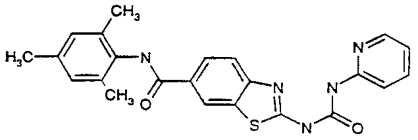
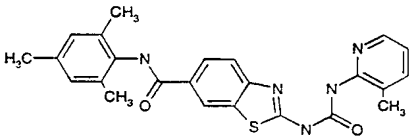
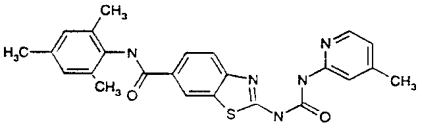
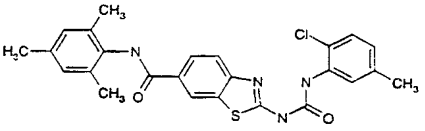
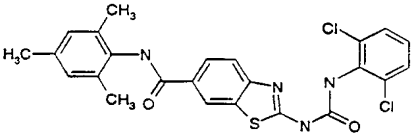
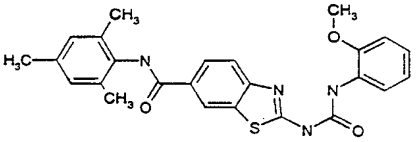
Compounds **59** to **95** were prepared following the procedure described below.

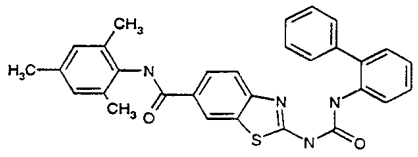
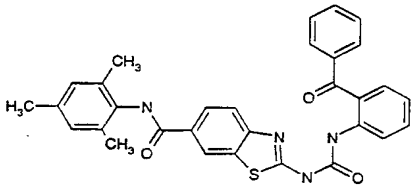
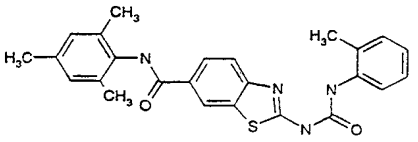
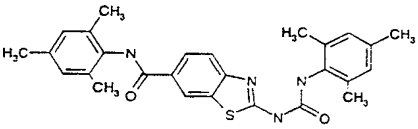
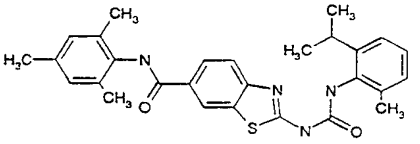
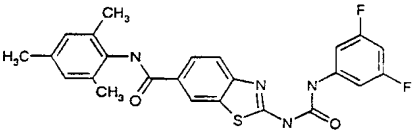
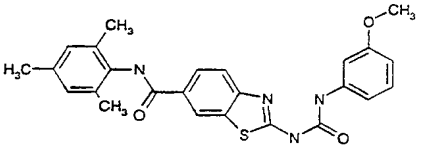
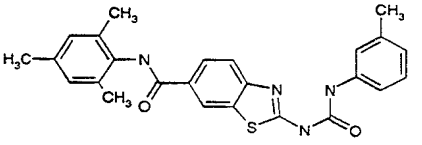
The appropriate arylamine (0.08 mmol) was added to a solution of **7A** (20 mg, 0.054 mmol) in THF (3 mL). The solution was heated to 45°C for 24 to 72 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (3 mL, 2x), and 1 N aq. NaOH solution (3 mL, 2x). The organic extract was dried ($MgSO_4$), filtered and concentrated *in vacuo* to obtain in crude form the compounds of these Examples, which were purified by HPLC (automated preparative HPLC under the following conditions: YMC ODS A 20x100 mm column, 10 minute gradient starting from 30% solvent B (90% MeOH, 10% H_2O, 0.1% TFA) and 70% solvent A (10% MeOH, 90% H_2O, 0.1% TFA) to 100% solvent B, flow rate 20 mL/min, λ = 220 nm), and are identified in Table 2 below.

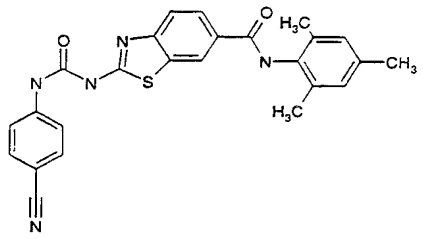
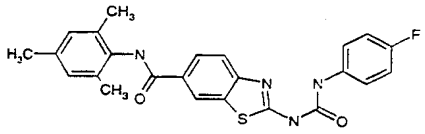
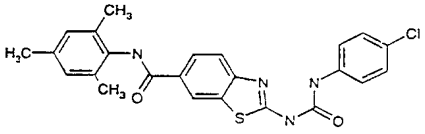
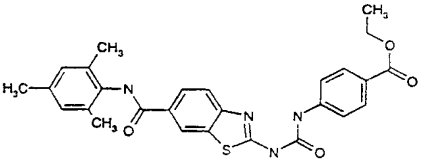
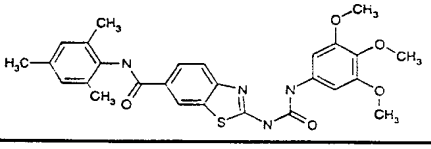
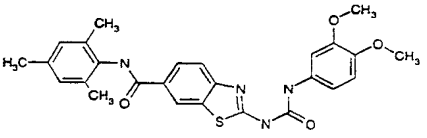
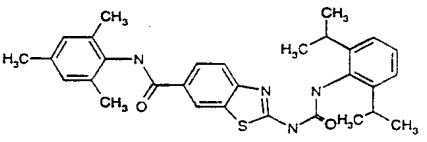
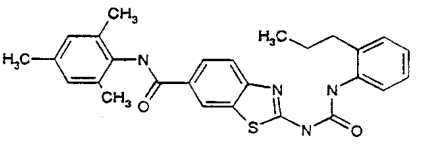
In Table 2, "HPLC Ret Time" was the HPLC retention time obtained under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 4 mL/min, λ = 220 nM.

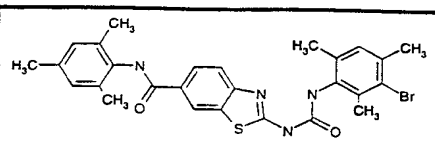
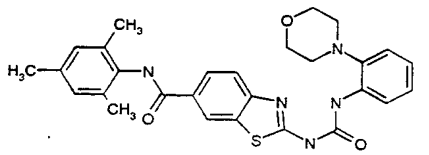
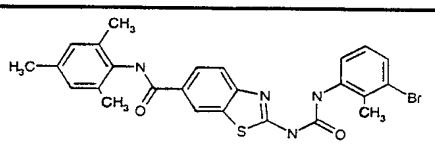
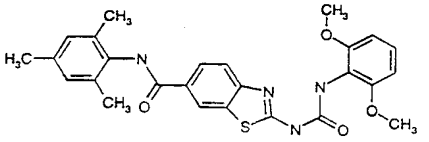
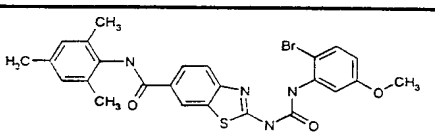
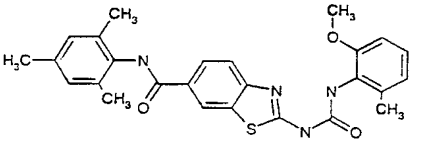
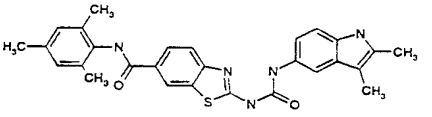
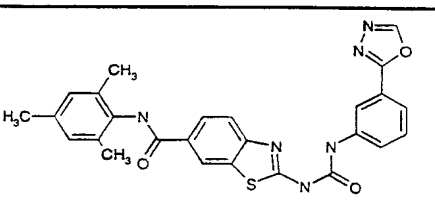
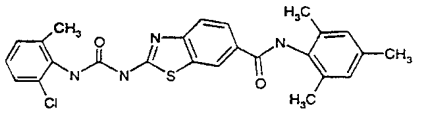
TABLE 2

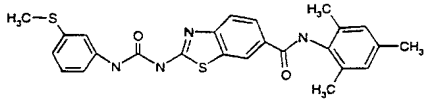
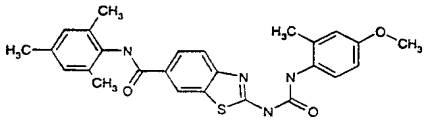
Ex. No.	Compound Structure	Compound Name	HPLC Ret Time (min)
59		2-[[[(4-Cyclohexylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.99

60		2-[[[(5,6,7,8-Tetrahydro-1-naphthalenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.64
61		2-[[[(2,3-Dihydro-1H-inden-5-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.94
62		2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.20
63		2-[[(2-Pyridinylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.95
64		2-[[[(3-Methyl-2-pyridinyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.75
65		2-[[[(4-Methyl-2-pyridinyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.89
66		2-[[[(2-Chloro-5-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.62
67		2-[[[(2,6-Dichlorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	5.03
68		2-[[[(2-Methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.37

69		2-[[([1,1'-Biphenyl]-2-ylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.57
70		2-[[[(2-Benzoylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.53
71		2-[[[(2-Methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.30
72		N-(2,4,6-Trimethylphenyl)-2-[[[(2,4,6-trimethylphenyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	4.35
73		2-[[[[2-Methyl-6-(1-methylethyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.42
74		2-[[[(3,5-Difluorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.23
75		2-[[[(3-Methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.25
76		2-[[[(3-Methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.38

77		2-[[[(4-Cyanophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.10
78		2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.27
79		2-[[[(4-Chlorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.47
80		4-[[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]benzoic acid, ethyl ester	4.50
81		2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.16
82		2-[[[(3,4-Dimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.10
83		2-[[[[2,6-Bis(1-Methylethyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	5.03
84		2-[[[(2-Propylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.52

85		2-[[[(3-Bromo-2,4,6-trimethylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.59
86		2-[[[[2-(4-Morpholinyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.70
87		2-[[[(3-Bromo-2-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.59
88		2-[[[(2,6-Dimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.91
89		2-[[[(2-Bromo-5-methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.61
90		2-[[[(2-Methoxy-6-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.10
91		2-[[[(2,3-Dimethyl-1H-indol-5-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.28
92		2-[[[[3-(1,3,4-Oxadiazol-2-yl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.76
93		2-[[[(2-Chloro-6-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.08

94		2-[[[[3-(Methylthio)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.48
95		2-[[[(4-Methoxy-2-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.59

Examples 96 to 140

General Procedure

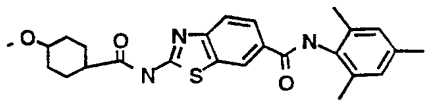
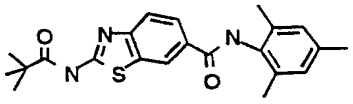
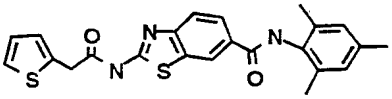
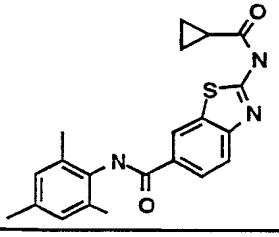
Compounds **96** to **140** were prepared following the procedure described below.

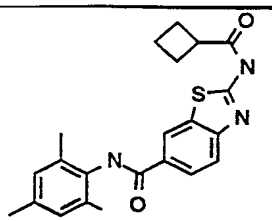
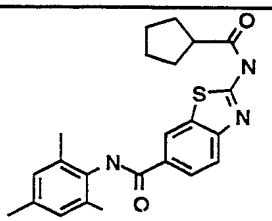
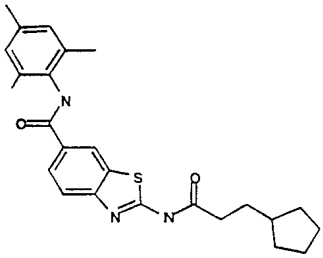
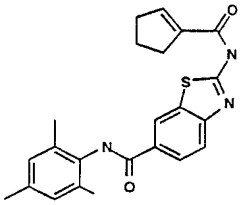
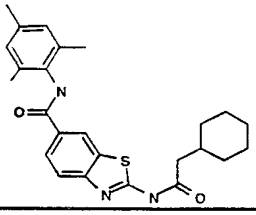
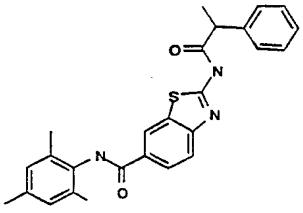
Diisopropylethyl amine (50 µL, 0.288 mmol) was added to a mixture of the free base of **2** (30 mg, 0.096 mmol), the appropriate carboxylic acid (0.115 mmol), 1-hydroxy-7-azabenzotriazole (17 mg, 0.125 mmol), and ethyl-3-(3-dimethylamino)-propyl carbodiimide hydrochloride (24 mg, 0.125 mmol) in THF (1 mL). The mixture was heated at 45°C for 18-72 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (2x), and 1 N aq. NaOH solution (2x). The organic extract was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude products were purified either by trituration with dichloromethane-ether or by automatic preparative HPLC (conditions: YMC ODS A 20x100 mm column, 10 minute gradient starting from 30% solvent B (90% MeOH, 10% H_2O, 0.1% TFA) and 70% solvent A (10% MeOH, 90% H_2O, 0.1% TFA) to 100% solvent B, flow rate 20 mL/min, λ = 220 nm) to obtain the compounds of these Examples which are identified in Table 3 below.

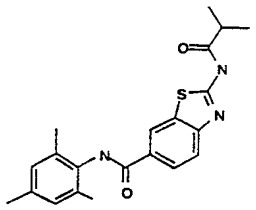
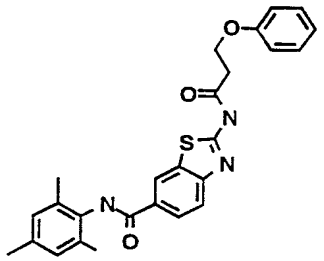
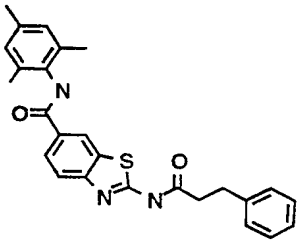
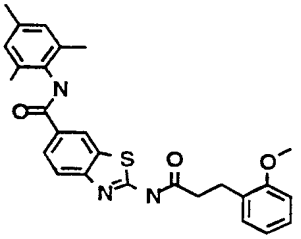
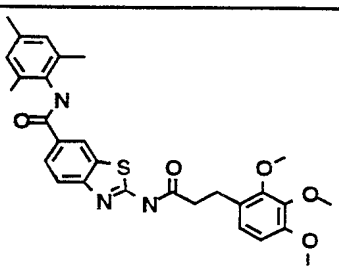
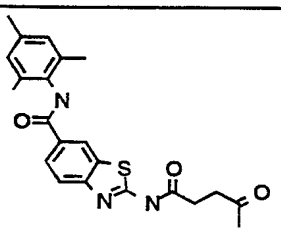
In Table 3, "HPLC Ret Time" was the HPLC retention time obtained under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O,

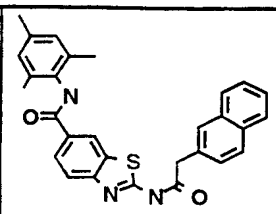
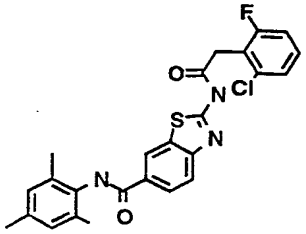
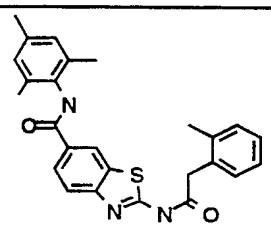
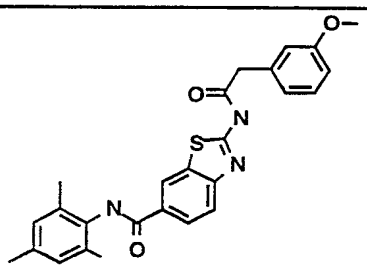
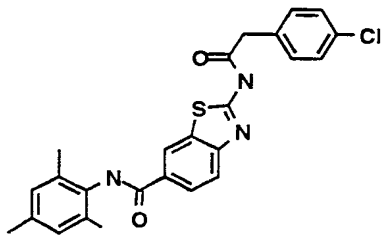
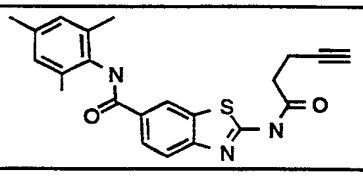
0.2% H_3PO_4), flow rate 4 mL/min, λ = 220 nM for compounds **99** to **140**. For compound **98** the HPLC conditions were: Zorbax SB-C18 4.5 mm x 7.5 cm short column, 8 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 2.5 mL/min, λ = 217 nM. For compound **96** the HPLC conditions were: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 3 mL/min, λ = 220 nM. For compound **97** the HPLC conditions were: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 8 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 3 mL/min, λ = 220 nM.

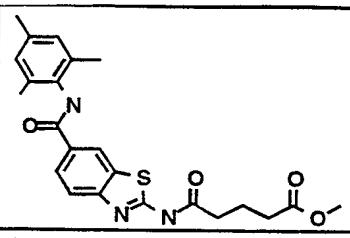
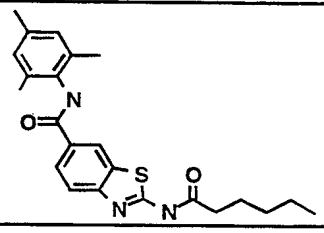
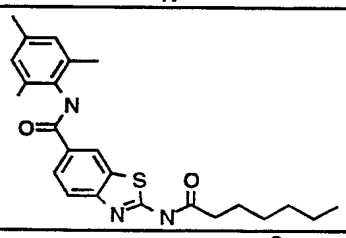
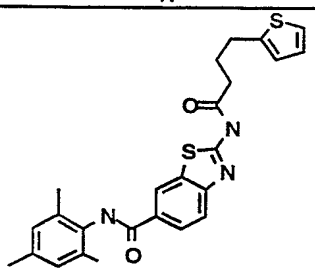
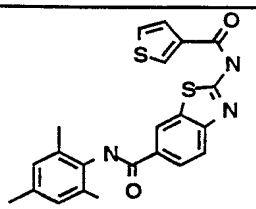
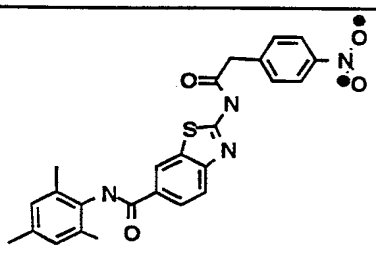
TABLE 3

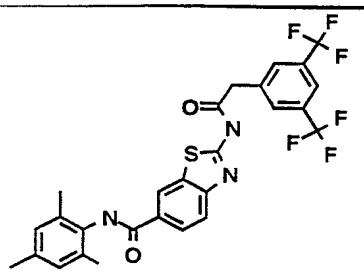
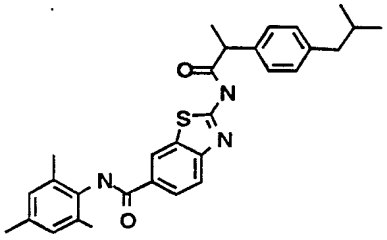
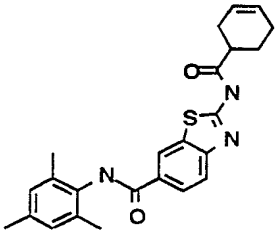
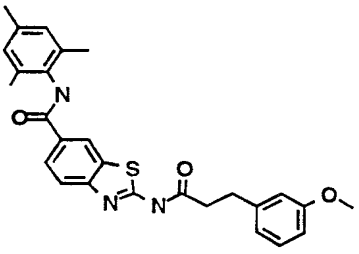
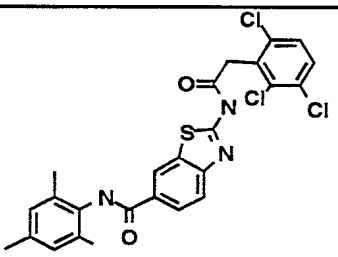
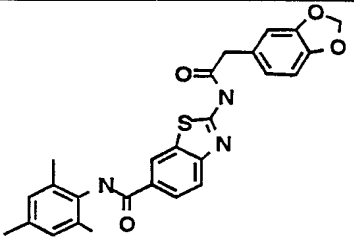
Ex. No.	Compound Structure	Compound Name	HPLC Ret Time (min)
96		2-[[(4-Methoxycyclohexyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.73
97		2-[(2,2-Dimethyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	8.62
98		2-[(2-Thienylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	8.58
99		2-[(Cyclopropylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.93

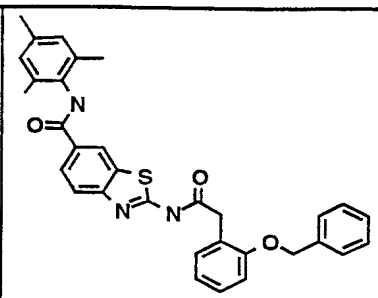
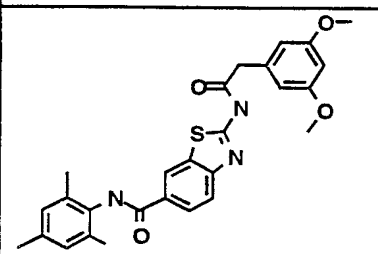
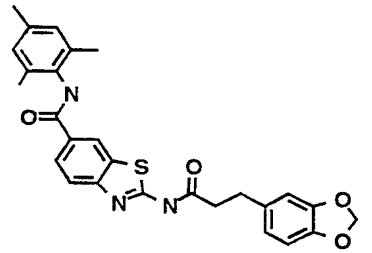
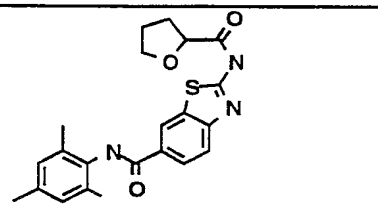
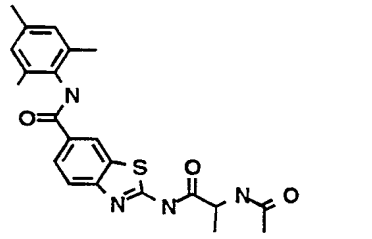
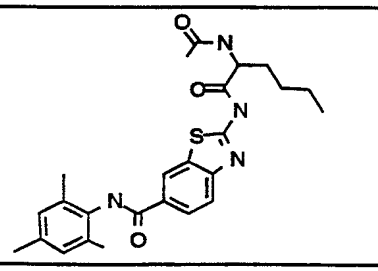
100		2-[(Cyclobutylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.00
101		2-[(Cyclopentylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.97
102		2-[(3-Cyclopentyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.52
103		2-[(1-Cyclopenten-1-ylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.27
104		2-[(Cyclohexylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.51
105		2-[(1-Oxo-2-phenylpropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.20

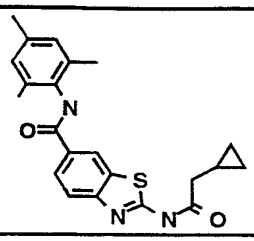
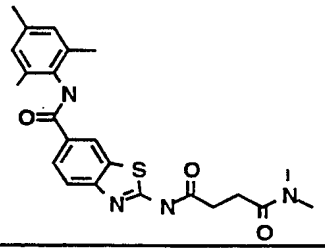
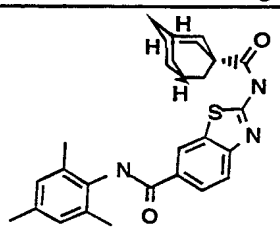
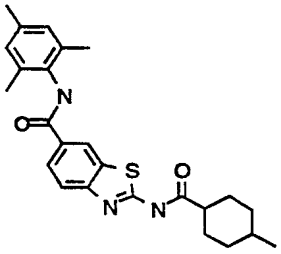
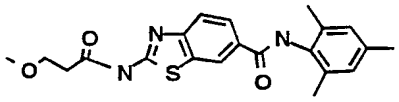
106		2-[(2-Methyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.89
107		2-[(1-Oxo-3-phenoxypropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.34
108		2-[(1-Oxo-3-phenylpropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.22
109		2-[[3-(2-Methoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.25
110		2-[[3-(2,3,4-Trimethoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.15
111		2-[(1,4-Dioxopentyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.98

112		2-[(2-Naphthalenylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.42
113		2-[[(2-Chloro-6-fluorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.21
114		2-[[(2-Methylphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.31
115		2-[[(3-Methoxyphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.07
116		2-[[(4-Chlorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.30
117		2-[(1-Oxo-4-pentynyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.76

118		5-Oxo-5-[[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]pentanoic acid, methyl ester	3.96
119		2-[(1-Oxohexyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.36
120		2-[(1-Oxoheptyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.49
121		2-[[1-Oxo-4-(2-thienyl)butyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.42
122		2-[(3-Thienylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.06
123		2-[[(4-Nitrophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.17

124		2-[[3,5-Bis(trifluoromethyl)phenyl]acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.65
125		2-[[2-[4-(2-Methypropyl)phenyl]-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.80
126		2-[[(3-Cyclohexen-1-yl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.20
127		2-[[3-(3-Methoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.22
128		2-[[(2,3,6-Trichlorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.50
129		2-[[(1,3-Benzodioxol-5-yl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.04

130		2-[[[2-(Phenylmethoxy)phenyl]acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.35
131		2-[[(3,5-Dimethoxyphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.09
132		2-[[3-(1,3-Benzodioxol-5-yl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.18
133		2-[[(Tetrahydro-2-furanyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.93
134		2-[[2-(Acetylamino)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.63
135		2-[[2-(Acetylamino)-1-oxohexyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.97

136		2-[(Cyclopropylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.92
137		N,N-Dimethyl-N'-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]butanediamide	3.66
138		2-[(1-Adamantylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.59
139		2-[[(4-Methylcyclohexyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.42
140		2-[(3-Methoxy-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	3.34

Examples 141 to 163

General Procedure

Compounds **141** to **163** were prepared following the procedure described below.

A. 2-*tert*-Butoxycarbonyloxyamino-benzothiazole-6-carboxylic acid chloride

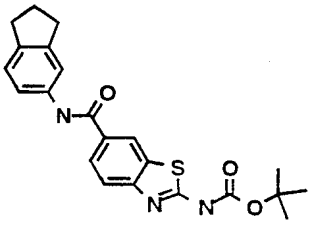
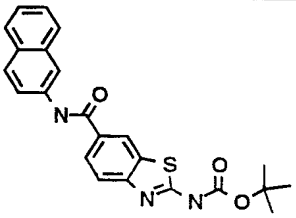
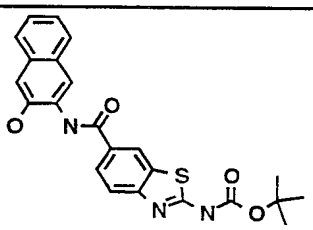
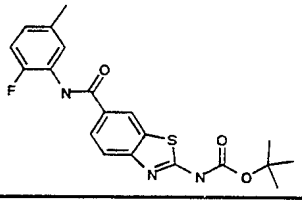
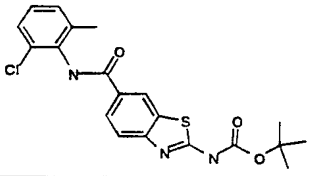
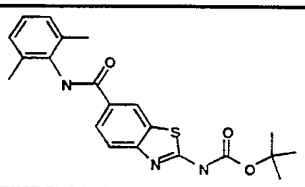
A 2 M solution of oxalyl chloride in dichloromethane (6.8 mL, 13.59 mmol) was added to a suspension of **1C** (2 g, 6.79 mmol) in dichloromethane (25 mL) at 0°C. Dimethylformamide (3 drops) was added. The ice bath was removed and the suspension was stirred at RT for 3 h and then heated to 32°C for an additional 3 h. The mixture was diluted with ether (25 mL) and the solid was collected by filtration. The solid was washed with ether several times, and dried *in vacuo* to obtain the title compound of this step (1.75 g, 82%). An additional crop of the title acid chloride was obtained by the trituration of the filtrate after concentration, with ether (250 mg, 12%).

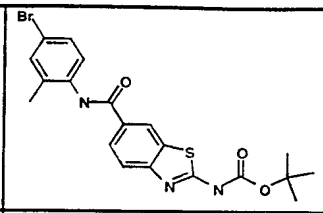
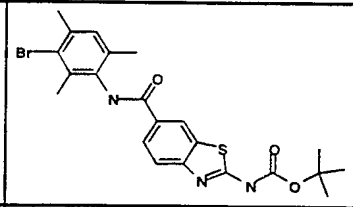
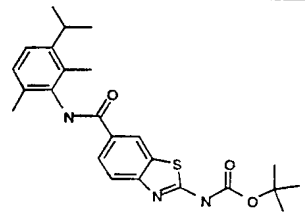
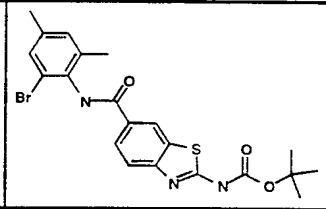
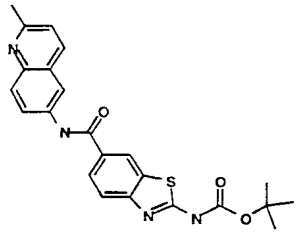
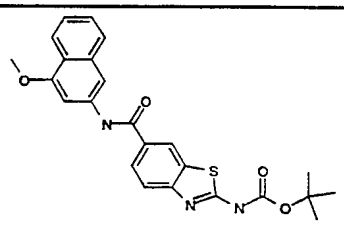
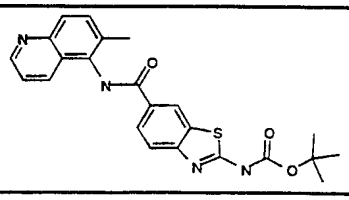
B. Compounds **141** to **163**

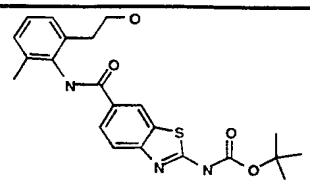
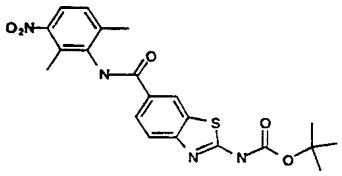
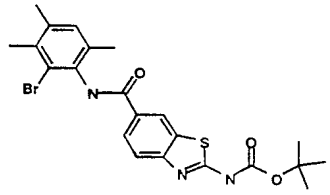
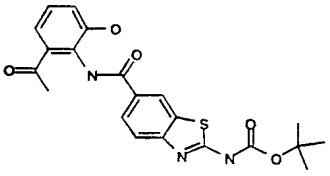
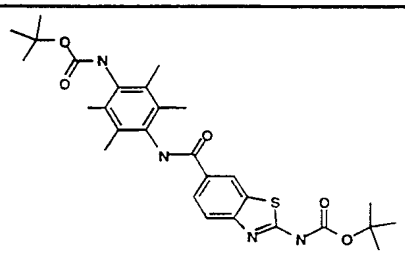
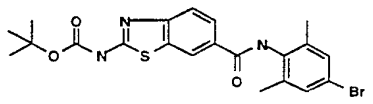
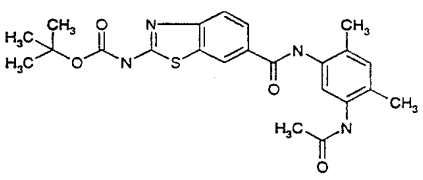
Diisopropylethyl amine (23 μL, 0.288 mmol) was added to a mixture of 2-*tert*-butoxycarbonyloxyamino-benzothiazole-6-carboxylic acid chloride (34.41 mg, 0.11 mmol), and the appropriate aniline (0.12 mmol) in THF (1 mL). The mixture was stirred at RT for 22 h. The reaction mixture was diluted with dichloromethane (4 mL) and washed with 2 N aq. HCl solution (2x), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude products were purified either by trituration with dichloromethane-ether (1:1) and/or by silica gel chromatography (eluting solvent: 2-5% MeOH in dichloromethane), and the compounds obtained in these Examples are identified in Table 4 below.

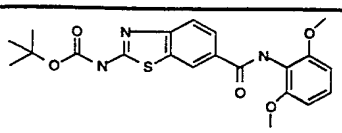
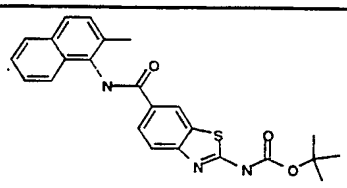
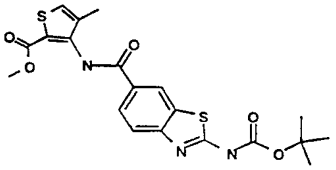
In Table 4, "HPLC Ret Time" was the HPLC retention time obtained under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 4 mL/min, λ = 220 nM.

TABLE 4

Ex. No.	Compound Structure	Compound Name	HPLC Ret Time (min)
141		[6-[[(2,3-Dihydro-1H-inden-5-yl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.44
142		[6-[(2-Naphthylenylamino)carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.46
143		[6-[[(3-Hydroxy-2-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.46
144		[6-[[(2-Fluoro-5-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.21
145		[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.05
146		[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.07

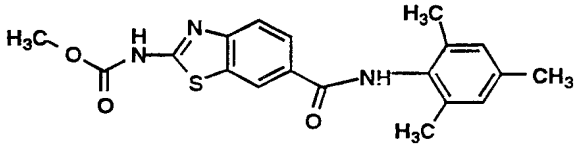
147		[6-[[(4-Bromo-2-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.34
148		[6-[[(3-Bromo-2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.45
149		[6-[[[2,6-Dimethyl-3-(1-methylethyl)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.44
150		[6-[[(2-Bromo-4,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.22
151		[6-[[(2-Methyl-6-quinolinyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	3.41
152		[6-[[(4-Methoxy-2-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.58
153		[6-[[(6-Methyl-5-quinolinyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	3.26

154		[6-[[[2-(2-Hydroxyethyl)-6-methylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	3.85
155		[6-[[(2,6-Dimethyl-3-nitrophenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.03
156		[6-[[(2-Bromo-3,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.32
157		[6-[[(2-Acetyl-6-hydroxyphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.26
158		[6-[[[4-[[(1,1-Dimethylethoxy)carbonyl]amino]-2,3,5,6-tetramethylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.31
159		[6-[[(4-Bromo-2,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	5.13
160		[6-[[[3-Acetylamino]-4,6-dimethylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.27

161		[6-[[(2,6-Dimethoxyphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	3.73
162		[6-[[(2-Methyl-1-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester	4.18
163		3-[[[2-[[(1,1-Dimethylethoxy)carbonyl]amino]-6-benzothiazolyl]carbonyl]amino]-4-methyl-2-thiophenecarboxylic acid, methyl ester	4.09

Example 164

Preparation of [6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, methyl ester

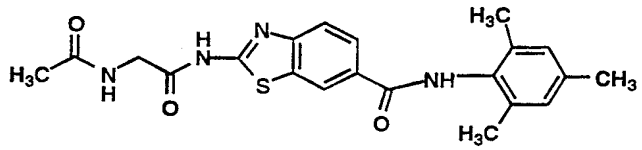


Methyl chloroformate (250 μL) was added dropwise to a stirred solution of the free base of **2** (62 mg, 0.2 mmol) in THF (10 mL) and 10% aq. $KHCO_3$ solution (15 mL) at 0 to 5°C. The biphasic mixture was stirred for 2 h, and then diluted with dichloromethane (25 mL) and water (20 mL). The organic extracts were dried ($MgSO_4$), filtered and concentrated. The crude residue was chromatographed on a silica gel column and eluted with 30% EtOAc in hexanes, followed by 50% and 70% EtOAc in hexanes, and 10% MeOH in dichloromethane to obtain the title compound (42 mg, 57%) as a white solid.

MS = 370 (M^+ + H)

Example 165

Preparation of 2-[[(Acetylamino)acetyl]aminol-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

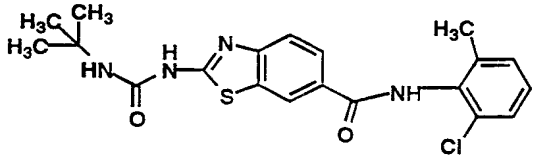


Diisopropylethyl amine (400 µL, 2.3 mmol) was added to a mixture of the free base of **2** (50 mg, 0.16 mmol), N-acetylglycine (42 mg, 0.36 mmol), 1-hydroxy-7-azabenzotriazole (49 mg, 0.36 mmol), and ethyl-3-(3-dimethylamino)-propyl carbodiimide hydrochloride (72 mg, 0.36 mmol) in THF (6 mL). The mixture was heated to 50°C overnight, cooled to RT, diluted with dichloromethane (60 mL) and washed with 2 N aq. HCl solution (20 mL), and satd. $NaHCO_3$ solution (15 mL, 2x). The dichloromethane extract was dried ($MgSO_4$), filtered and concentrated. The residue was diluted with dichloromethane-methanol (20 mL, 4:1) and EtOAc (5 mL) was added. The precipitated solid was filtered, washed with EtOAc (5 mL, 3x), and dried *in vacuo* to obtain the title compound of this Example (15 mg, 22.8%).

MS = 411.1 (M^+ + H)

Example 166

Preparation of N-(2-Chloro-6-methylphenyl)-2-[[[(1,1-dimethylethyl)aminolcarbonyl]aminol-6-benzothiazolecarboxamide



A. Ethyl-2-[[(phenoxy)carbonyl]amino]-benzothiazole-6-carboxylate

Phenyl chloroformate (14.25 mL, 113.6 mmol) was added dropwise to a stirred solution of **1A** (8.6 g, 37.86 mmol) in THF (300 mL) and satd. aq. $KHCO_3$ solution (300 mL) at 0 to 5°C. The biphasic mixture was stirred for 3.5 h. The THF layer was separated and the aq. layer was extracted with dichloromethane (150 mL, 2x). A yellow solid which precipitated during the work up was collected by filtration, washed with dichloromethane, water and ether. Organic extracts were combined, dried (Na_2SO_4), filtered and concentrated to obtain a yellow solid. The crude solids were combined, diluted with ether (100 mL), filtered, and dried *in vacuo* to obtain the title compound of this step as a yellow solid (11.24 g, 85%).

B. Ethyl-2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-benzothiazole-6-carboxylate

tert-Butyl amine (6.66 mL, 63.4 mmol) was added to a stirred suspension of **166A** (11.23 g, 32.33 mmol) in THF (163 mL). The suspension was stirred at RT for 16 h, and the yellow solid was filtered, washed with THF, 2 N aq. HCl solution, 0.1 N aq. NaOH solution, water and ether. The filtrate was diluted with dichloromethane and washed with 2 N aq. HCl solution (2x) and 0.1 N aq. NaOH solution (2x) and brine. The dichloromethane extract was dried (Na_2SO_4), filtered and concentrated to obtain a yellow solid. Solids were combined, suspended in ether, filtered, washed several times with ether and dried *in vacuo* to obtain the title compound of this step (10.41 g, 100%).

C. 2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-benzothiazole-6-carboxlic acid

An aq. 2 N potassium hydroxide solution (405 mL) was added to a suspension of **166B** (10.41 g, 32.4 mmol) in THF (90 mL) and ethanol (135 mL). The mixture was heated to 60°C, cooled to 0°C and concentrated. The residue was cooled to 0°C and acidified to pH 1.0 with conc. HCl solution. The precipitated solid was filtered, washed with water and

ether. The solid was suspended in toluene (2x) and concentrated under reduced pressure. This operation was repeated with ether (2x). The solid was collected and dried *in vacuo* over phosphorus pentoxide to obtain the title acid of this step (10 g , 100% yield).

D. 2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-benzothiazole-6-carboxylic acid-7-aza-benzotriazole ester ("HOAT ester")

Diisopropylethyl amine (958 μL, 6.84 mmol) was added to a solution of **166C** (500 mg, 1.71 mmol), and HATU (778 mg, 2.05 mmol) in dimethylformamide (10 mL). The solution was stirred at RT overnight, diluted with dichloromethane and washed with 1 N aq. HCl solution and water. The dichloromethane extract was separated, dried ($MgSO_4$) and concentrated. The crude solid was triturated with methanol (2x) to obtain the title compound of this step (380 mg, 54.3%). A second crop of the title compound (152 mg, 21.7%) was obtained after trituration of the residual filtrate.

E. N-(2-Chloro-6-methylphenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide

A 1 M solution of sodium bis-trimethylsilyl amide (366 μL, 0.37 mmol) was added to a stirred solution of 2-chloro-6-methylaniline (33.1 μL, 0.268 mmol) in THF (2 mL). The mixture was stirred at RT for 10 min, and **166D** (100 mg, 0.244 mmol) was added. Dimethylformamide (2 mL) was added to dissolve the precipitate obtained during the reaction. The mixture was stirred at RT overnight, diluted with dichloromethane and washed with 1 N aq. HCl solution (30 mL, 3x), 5% aq. $KHCO_3$ solution (20 mL, 2x). The organic extract was dried ($MgSO_4$), filtered and concentrated. The crude residue was purified by automated preparative HPLC (conditions: YMC ODS A 20x100 mm column, 10 minute gradient starting from 30% solvent B (90% MeOH, 10% H_2O, 0.1% TFA) and 70% solvent A (10% MeOH, 90% H_2O, 0.1% TFA) to 100%

solvent B, flow rate 20 mL/min, λ = 220 nm) to obtain the title compound of this Example (19.5 mg, 19%).
MS = 417 (M^+ + H)

Alternative method

A(Alt). [6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

Diisopropylethyl amine (1.67 mL, 6.02 mmol) was added to a stirred suspension of **141A** [2-*tert*-butoxycarbonyloxyamino-benzothiazole-6-carboxylic acid chloride] (1.88 g, 6.02 mmol), 2-chloro-6-methylaniline (960 µL, 7.83 mmol) in THF (40 mL). The mixture was stirred at RT overnight and then diluted with dichloromethane (100 mL). The reaction mixture was washed with 1 N aq. HCl solution (2x), 1 N aq. NaOH solution, and brine. The organic layer was dried (Na_2SO_4), filtered, and concentrated. The residue was diluted with EtOAc (10 mL), stirred for 20 min, and diethyl ether (5 mL) was added. After 5 min, the solid was filtered, and dried *in vacuo* to obtain the title compound of this step (940 mg, 37%).

B(Alt). 2-Amino-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide

A solution of **166A(Alt)** (940 mg, 2.25 mmol) in trifluoroacetic acid (5 mL) and dichloromethane (2 mL) was stirred at RT overnight. The mixture was concentrated, diluted in dichloromethane (100 mL), and washed with satd. sodium bicarbonate solution (2x), water and brine. The dichloromethane extract was dried (Na_2SO_4), filtered, and concentrated *in vacuo* to obtain the title compound of this step (750 mg, 98%).

C(Alt). [6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, phenyl ester

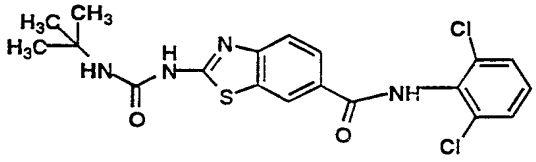
Analogous to the preparation of Example **7A** except using **166B(Alt)** in place of the free base of **2** gave the title compound of this step (92%) after trituration with diethyl ether/EtOAc (1:1).

D(Alt). N-(2-Chloro-6-methylphenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide

A solution of **166C(Alt)** (680 mg, 1.57 mmol) and tert-butyl amine (196 μL, 1.87 mmol) in THF (50 mL) was stirred for 7 h. The mixture was diluted with dichloromethane (200 mL) and washed with 1 N aq. HCl solution (50 mL), 1 N aq. NaOH solution (50 mL, 2x). The organic extract was dried (Na_2SO_4), filtered, and concentrated. The residue was triturated with diethyl ether to obtain the title compound of this Example (488 mg, 75%).

Example 167

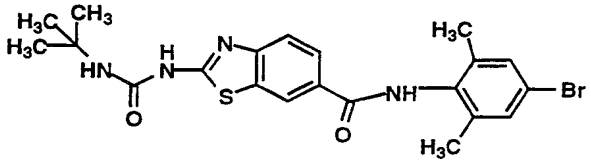
Preparation of N-(2,6-Dichlorophenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide



Analogous to the preparation of compound **166E** except using 2,6-dichloroaniline gave the title compound (17%) after purification by automated preparative HPLC (conditions: YMC ODS A 20x100 mm column, 10 minute gradient starting from 30% solvent B (90% MeOH, 10% H_2O, 0.1% TFA) and 70% solvent A (10% MeOH, 90% H_2O, 0.1% TFA) to 100% solvent B, flow rate 20 mL/min, λ = 220 nm).
MS = 438 (M^+ + H)

Example 168

Preparation of N-(4-Bromo-2,6-dimethylphenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide

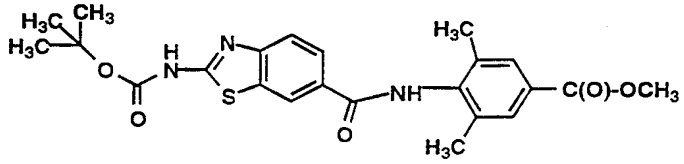


Analogous to the preparation of compound **166E** except using 4-bromo-2,6-dimethylaniline gave the title compound (19%) after purification by automated preparative HPLC (conditions: same as in Example 167).

MS = 477 (M^+ + H)

Example 169

Preparation of N-(4-Carbomethoxy-2,6-Dimethylphenyl)-2-[[[1,1-dimethylethoxy]carbonyl]amino]-6-benzothiazolecarboxamide

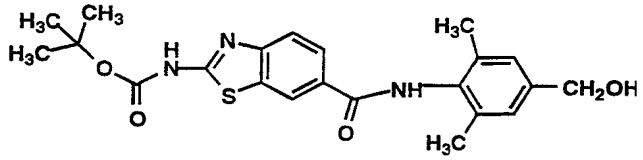


Analogous to the preparation of the compounds of Table 4 using 4-carbomethoxy-2,6-dimethylaniline gave the title compound of this Example (53%).

MS = 428.1 (M^+ + H)

Example 170

Preparation of N-(4-Hydroxymethyl-2,6-Dimethylphenyl)-2-[[[1,1-dimethylethoxy]carbonyl]amino]-6-benzothiazolecarboxamide

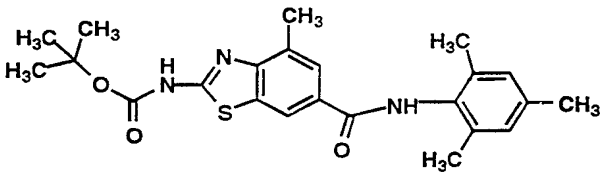


Analogous to the preparation of compounds **141** to **163** except using 4-hydroxymethyl-2,6-dimethylaniline gave the title compound of this Example (71%).

MS = 456.1 (M^+ + H)

Example 171

Preparation of [4-Methyl-6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



A. Methyl-2-amino-4-methyl-benzothiazole-6-carboxylate

Analogous to the preparation of compound **1A** except using methyl-4-amino-3-methylbenzoate gave the title compound of this step.

B. Methyl-2,2-bis-*tert*-butoxycarbonyloxyamino-4-methyl-benzothiazole-6-carboxylate

A suspension of **171A** (1.16 g, 5.2 mmol, 85% pure), di-t-butylcarbonate (2.37 g, 10.87 mmol) and 4-dimethylaminopyridine (93 mg, 0.76 mmol) in THF (80 mL) was heated to 60°C for 3.5 h. The mixture was cooled, washed with 1 N aq. HCl solution (50 mL, 2x), and water. The organic extract was dried ($MgSO_4$), filtered and concentrated to obtain the title compound of this step (693 mg, 31.5%).

C. 2-*tert*-Butoxycarbonyloxyamino-4-methyl-benzothiazole-6-carboxylic acid

Analogous to the preparation of **1C** except using **171B** gave the title compound (95%) of this step as a white solid.

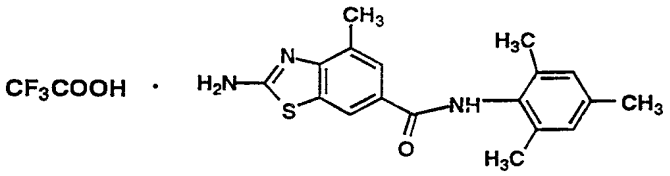
D. [4-Methyl-6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

Diisopropylethyl amine (65 μL, 0.51 mmol) was added to a stirred solution of **171C** (50 mg, 0.17 mmol), 2,4,6-trimethylaniline (28.4 μL, 0.203 mmol) and benzotriazolo-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (Castro's reagent, 89.6 mg, 0.203 mmol) in dimethylformamide (2 mL). The solution was stirred at RT for 40 h and then diluted with dichloromethane (50 mL). The mixture was washed with 1 N aq. HCl solution (25 mL, 2x) and water, dried ($MgSO_4$), filtered and concentrated. The crude residue was triturated with a mixture of ether and EtOAc. Solid was collected and dried *in vacuo* to obtain the title compound of this Example (43 mg, 62%).

MS = 426 (M^+ + H)

Example 172

Preparation of 2-Amino-4-methyl-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1)

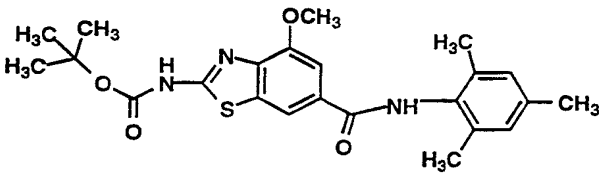


Analogous to the preparation of compound **2** except using **171D** afforded the title compound of this Example (74%).

MS = 326 (M^+ + H)

Example 173

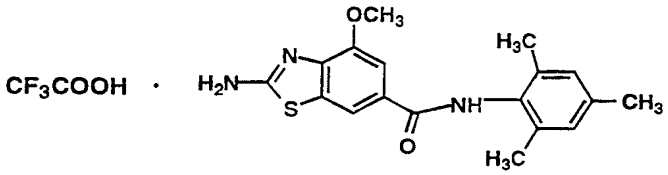
Preparation of 4-Methoxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



Analogous to the preparation of **171D** except using methyl-4-amino-3-methoxybenzoate gave the title compound of this Example.
MS = 442 (M^+ + H)

Example 174

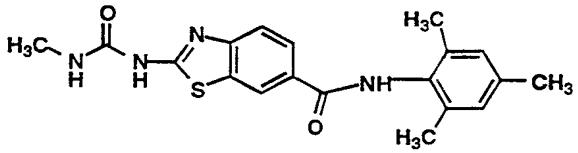
Preparation of 2-Amino-4-methoxy-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1)



Analogous to the preparation of **2** except using **173** afforded the title compound (82%) as a white solid.
MS = 342 (M^+ + H)

Example 175

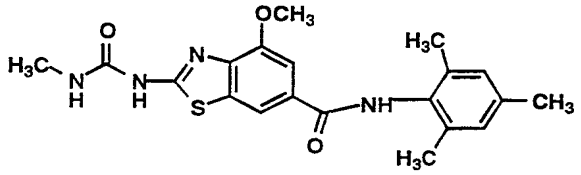
Preparation of 2-[[(Methylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **15** except using methyl isocyanate gave the title compound (71%) as a white solid.
MS = 369 (M^+ + H)

Example 176

Preparation of 2-[[[Methylamino]carbonyl]amino]-4-methoxy-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

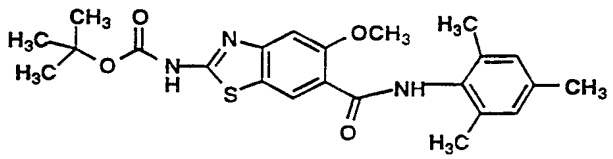


Analogous to the preparation of **175** except using **174** gave the title compound (39%) as a white solid.

MS = 399 (M^+ + H)

Example 177

Preparation of 5-Methoxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

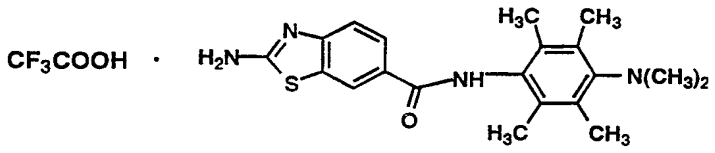


Analogous to the preparation of **171D** except using methyl-4-amino-2-methoxybenzoate gave the title compound of this Example.

MS = 442 (M^+ + H)

Example 178

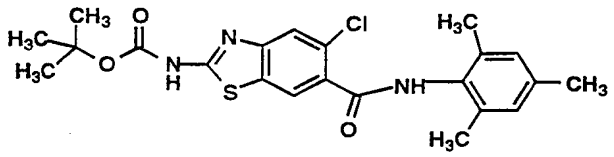
Preparation of 2-Amino-N-(4-N,N-dimethylamino-2,3,5,6-tetramethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1)



Analogous to the preparation of the compounds of Table 4 using using N_1,N_1,2,3,5,6-hexamethyl-1,4-phenylenediaminedihydrochloride gave the title compound of this Example after purification by automated preparative HPLC (conditions: same as in Example 167).
MS =369.2 (M^+ + H)

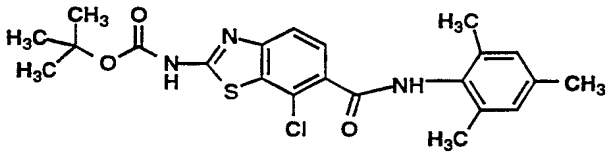
Examples 179 and 180

Preparation of 5-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester (**179**)



and

7-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester (**180**)



A. Methyl-2-amino-5-chloro-benzothiazole-6-carboxylate (**179A**) and Methyl-2-amino-7-chloro-benzothiazole-6-carboxylate (**180A**)

Analogous to the preparation of compound **1A** except using methyl-2-amino-4-chlorobenzoate gave a mixture of the title compounds **179A** and **180A** in 2:1 ratio (71%).

B. Methyl-2-*tert*-butoxycarbonyloxyamino-5-chloro-benzothiazole-6-carboxylate (**179B**) and Methyl-2-*tert*-butoxycarbonyloxyamino-7-chloro-benzothiazole-6-carboxylate (**180B**)

Analogous to the preparation of compound **1B** except using a mixture of compounds **179A** and **180A** gave a mixture of the title compounds **179B** and **180B** (2:1) as a yellow solid (63%).

C. 2-*tert*-Butoxycarbonyloxyamino-5-chloro-benzothiazole-6-carboxylic acid (**179C**) and 2-*tert*-Butoxycarbonyloxyamino-7-chloro-benzothiazole-6-carboxylic acid (**180C**)

A solution of a mixture of compounds **179B** and **180B** (3.75 g, 10.9 mmol) in ethanol (50 mL) and 2 N aq. sodium hydroxide solution (27.5 mL, 55 mmol) was stirred at RT for 18 h. Most of the ethanol was removed *in vacuo* and the residue was cooled to 0°C and acidified with satd. aq. potassium hydrogen sulfate to pH 1-2. The precipitate was filtered, washed with water and dried *in vacuo* to obtain a mixture of the title acids **179C** and **180C** (4.3 g, 100%, 2:1 ratio) as a yellow solid.

D. 5-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester (**179D**) and 7-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester (**180D**)

Diisopropylethyl amine (400 µL, 2.2 mmol) was added to a stirred suspension of compounds **179C** and **180C** (328 mg, 1 mmol), 2,4,6-trimethylaniline (170 µL, 1.1 mmol) and benzotriazolo-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (Castro's reagent, 485 mg, 1.1 mmol) in dichloromethane (5 mL). The solution was stirred at RT for 18 h, filtered and dried to obtain a mixture of intermediate benzotriazolo-esters (400 mg) which was dissolved in

dimethylformamide (5 mL) and 2,4,6-trimethylaniline (560 µL, 4 mmol) was added. The solution was heated to 50°C for 72 h, cooled and diluted with EtOAc (100 mL) and water (100 mL). The EtOAc layer was separated, washed with 1 N aq. HCl solution (100 mL, 3x), brine (50 mL), dried ($MgSO_4$), filtered and concentrated. The orange-yellow solid was dissolved in dimethylsulfoxide (1 mL) and diluted with methanol (5 mL), followed by water (5 mL). The solution was let stand at RT for several hours. The precipitated solid was filtered, washed with water (20 mL), dried and then recrystallized from DMSO - MeOH - H_2O mixture to obtain the pure title compound **179D** (45 mg, 10%).

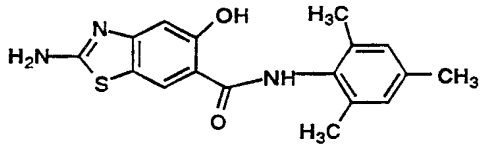
MS = 447 (M^+ + H)

A second crop of solid was obtained from the mother liquor which was collected by filtration and dried *in vacuo* to obtain the title compound **180D** (44 mg, 10%).

MS = 447 (M^+ + H)

Example 181

Preparation of 2-Amino-5-hydroxy-N-[2,4,6-trimethylphenyl]-6-benzothiazolecarboxamide

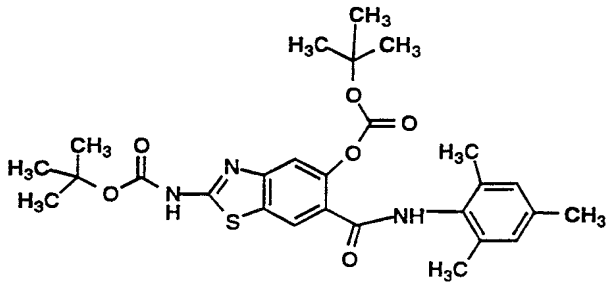


Boron tribromide (300 µL, 3 mmol) was added to a solution of **177** (441 mg, 1 mmol) in dichloromethane (7 mL) at -78°C. The solution was stirred at -78°C for 1 h and at RT for 1 h, diluted with satd. aq. $NaHCO_3$ solution and concentrated *in vacuo*. The residue was diluted with water and filtered. The white solid was washed thoroughly with water, ether and dried *in vacuo* to obtain the title compound of this Example (260 mg, 80%).

MS = 328 (M^+ + H)

Example 182

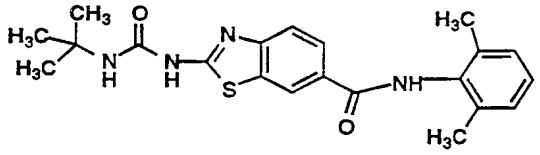
Preparation of 5-*tert*-Butoxycarbonyloxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



Analogous to the preparation of **1B** except using **181** afforded the title compound **182** (25%) after purification by silica gel chromatography and elution with a gradient of dichloromethane to 5% MeOH in dichloromethane in 1% increment with MeOH.
MS = 428 (M^+ + H)

Example 183

Preparation of 2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **166E** except using 2,6-dimethylaniline gave the title compound (19%) after purification by automated preparative HPLC (conditions: same as in Example 167).
MS = 397 (M^+ + H)

Alternative method

A(Alt). [6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester

Diisopropylethyl amine (1.17 mL, 6.42 mmol) was added to a stirred suspension of **141A** [2-*tert*-butoxycarbonyloxyamino-benzothiazole-6-carboxylic acid chloride] (1 g, 3.21 mmol), 2,6-dimethylaniline (473 µL, 3.84 mmol) in THF (25 mL). The mixture was stirred at RT overnight and then diluted with dichloromethane (70 mL). The reaction mixture was washed with 1 N aq. HCl solution (30 mL, 2x), water and brine. The organic layer was dried (Na_2SO_4), filtered, and concentrated. The residue was triturated with diethyl ether/EtOAc (1:1), filtered, and dried *in vacuo* to obtain the title compound of this step (475 mg, 37%).

B(Alt). 2-Amino-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide

A solution of **183A(Alt)** (1 g, 2.5 mmol) in trifluoroacetic acid (6 mL) and dichloromethane (5 mL) was stirred at RT for 2.5 h. The mixture was concentrated, dissolved in dichloromethane and washed with satd. sodium bicarbonate solution (25 mL, 2x), water and brine. The dichloromethane extract was dried (Na_2SO_4), filtered, and concentrated. The residue was triturated with ether to obtain the title compound of this step (570 mg, 76%).

C(Alt). [6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, phenyl ester

Analogous to the preparation of Example **7A** except using **183B(Alt)** in place of the free base of **2** gave the title compound of this step (98%) after trituration with diethyl ether/EtOAc (10:1).

D(Alt). 2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide

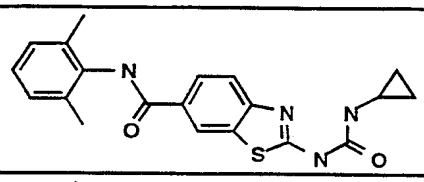
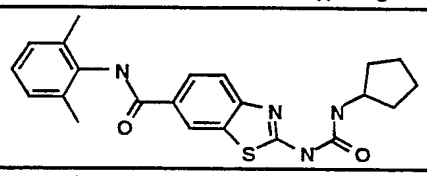
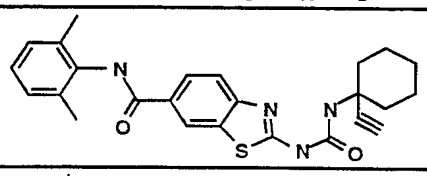
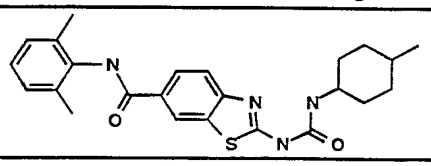
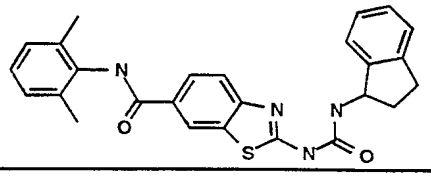
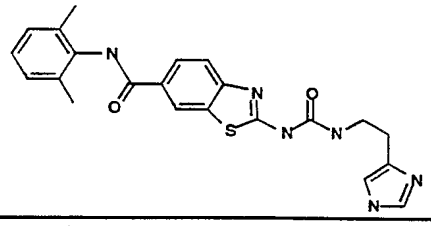
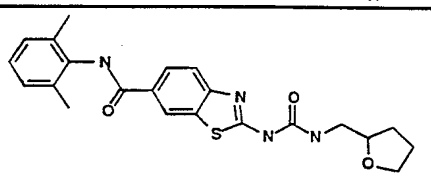
A solution of **183C(Alt)** (46 mg, 0.11 mmol) and tert-butyl amine (14 μL, 0.13 mmol) in THF (4 mL) was stirred at RT overnight. The mixture was diluted with dichloromethane (50 mL) and washed with 1 N aq. HCl solution (30 mL), 1 N aq. NaOH solution (25 mL, 2x), water. The organic extract was dried (Na_2SO_4), filtered, and concentrated. The residue was triturated with diethyl ether to obtain the title compound of this Example (23 mg, 66%).

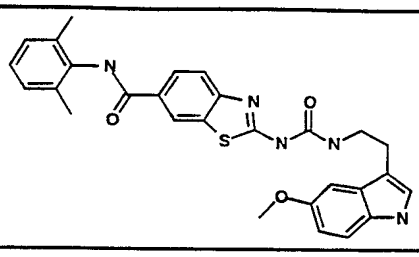
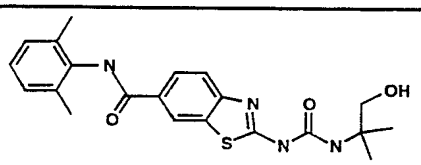
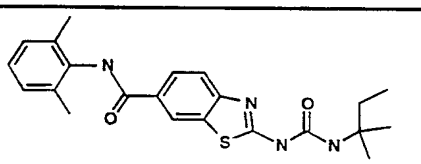
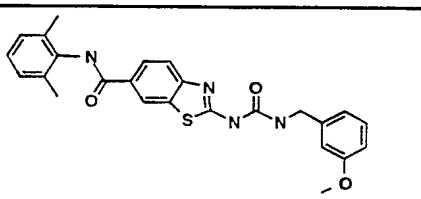
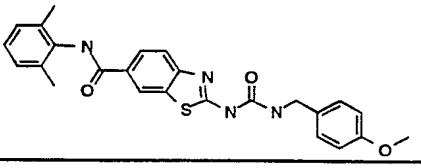
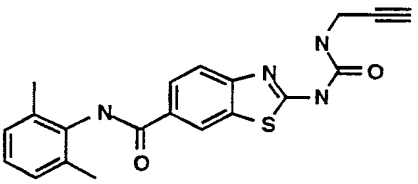
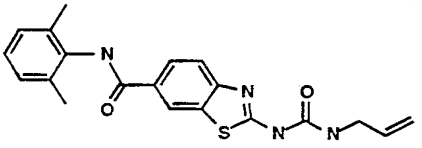
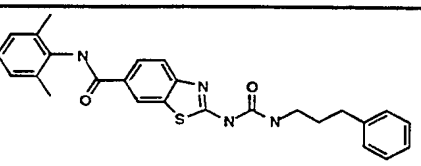
Examples 184 to 204

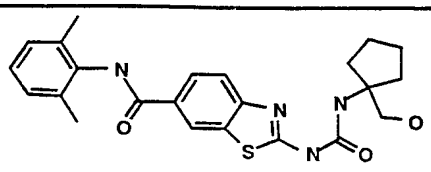
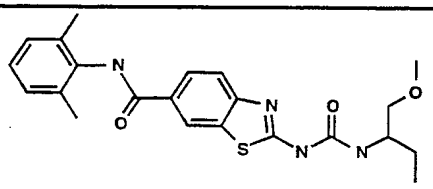
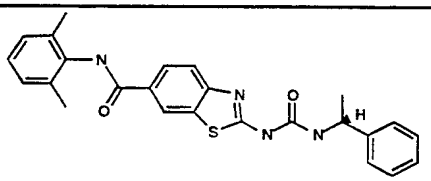
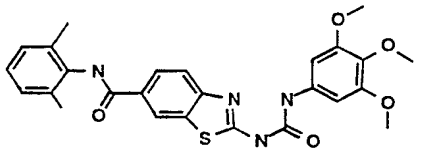
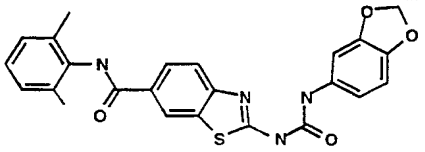
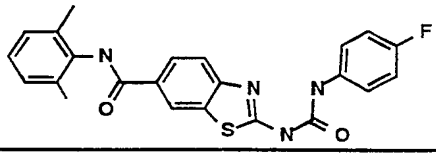
General Procedure

Compounds **184** to **204** were prepared following the procedure described below.

The appropriate amine (0.086 mmol) was added to a solution of **183C(Alt)** (30 mg, 0.072 mmol) in THF (3 mL). In the case of aliphatic amines, the solution was stirred at RT for 48-72 h. For anilines, the solution was heated to 60°C for 72 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (2x), 1 N aq. NaOH solution (2x). The organic extract was dried (Na_2SO_4), filtered and concentrated *in vacuo* to obtain the title compounds of these Examples. Some of the title compounds required purification achieved by automated preparative HPLC under the following conditions: YMC ODS 20 x 100 mm Column, 10 min gradient starting from 70% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) and 30% solvent B to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 20 mL/min, λ = 220 nM. "HPLC Ret Time" is the HPLC retention time under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 4 mL/min, λ = 220 nM.

Ex. No.	Compound Structure	Compound Name	HPLC Ret Time (min)
184		2-[[(Cyclopropylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.62
185		2-[[(Cyclopentylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.04
186		2-[[[[1-(ethynyl)cyclohexyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.13
187		2-[[[(4-Methyl-cyclohexyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.39
188		2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.25
189		2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	2.84
190		2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.68

191		2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.99
192		2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.07
193		2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.14
194		2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.02
195		2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2, 6-dimethylphenyl)-6-benzothiazolecarboxamide	4.00
196		2-[[(2-Propynylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.06
197		2-[[(2-Propenylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.69
198		2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.29

199		2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.90
200		2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.86
201		(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.12
202		2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.15
203		2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.02
204		2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.05

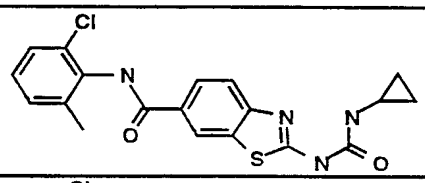
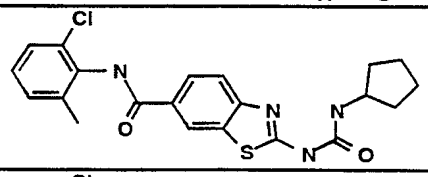
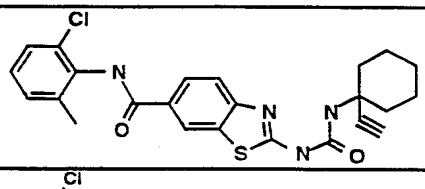
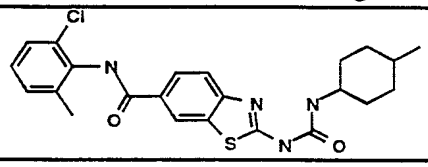
Examples 205 to 226

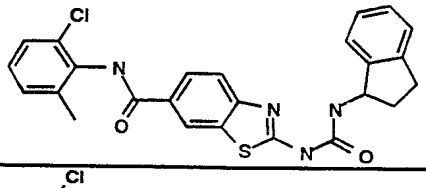
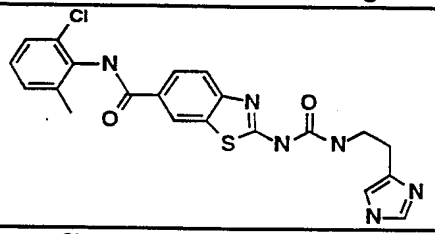
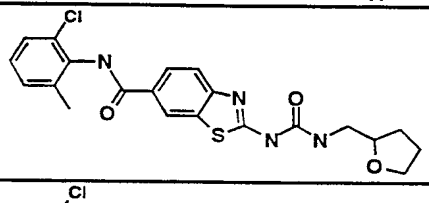
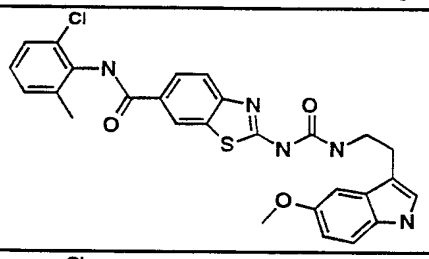
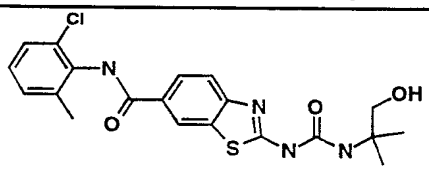
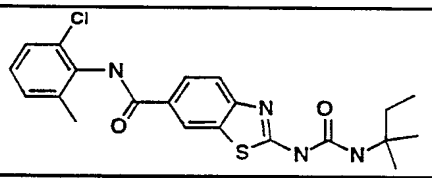
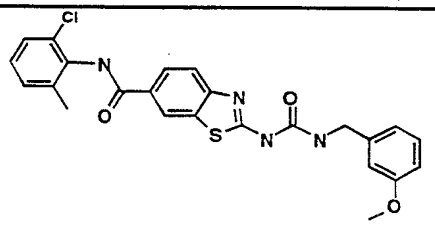
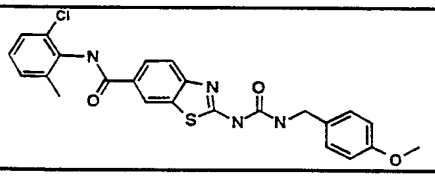
General Procedure

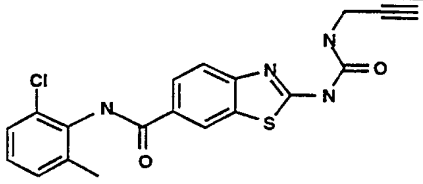
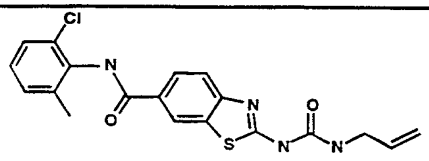
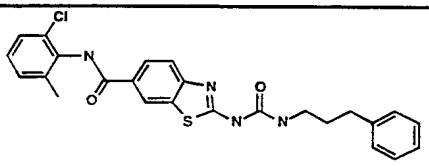
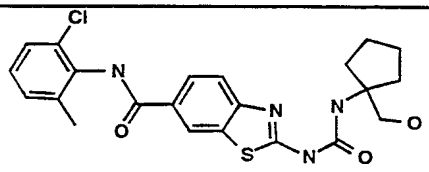
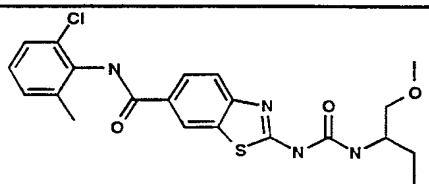
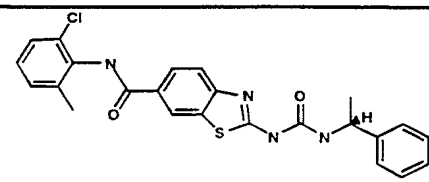
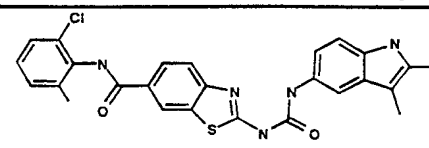
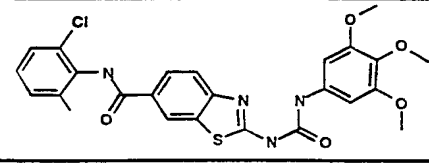
Compounds **205** to **226** were prepared following the procedure described below.

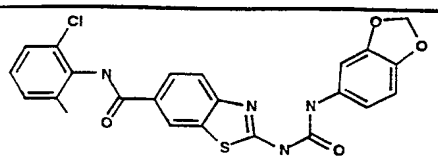
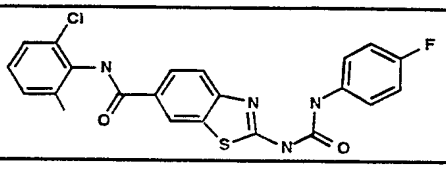
The appropriate amine (0.086 mmol) was added to a solution of **166C(Alt)** (30 mg, 0.072 mmol) in THF (3 mL). In case of the aliphatic amines, the solution was stirred at RT for 48-72 h. For anilines, the solution was heated to 60°C for 72 h. The reaction mixture was diluted

with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (2x), 1 N aq. NaOH solution (2x). The organic extract was dried (Na_2SO_4), filtered and concentrated *in vacuo* to obtain the title compounds of these Examples. Some of the title compounds required purification achieved by automated preparative HPLC under the following conditions: YMC ODS 20 x 100 mm Column, 10 min gradient starting from 70% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) and 30% solvent B to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 20 mL/min, λ = 220 nM. "HPLC Ret Time" is the HPLC retention time under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 4 mL/min, λ = 220 nM.

Ex. No.	Compound Structure	Compound Name	HPLC Ret Time (min)
205		2-[[(Cyclopropylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.15
206		2-[[(Cyclopentylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.08
207		2-[[[[1-(ethynyl)cyclohexyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.17
208		2-[[[(4-Methyl-cyclohexyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.37

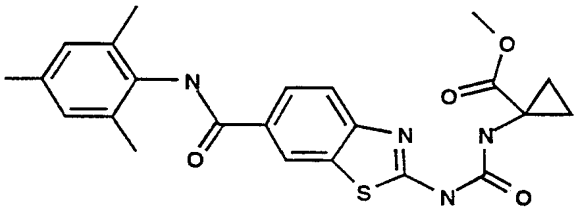
209		2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.23
210		2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.87
211		2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.00
212		2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	3.97
213		2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.29
214		2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.12
215		2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.01
216		2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	3.98

217		2-[[(2-Propynylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.37
218		2-[[(2-Propenylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	3.67
219		2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.27
220		2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.28
221		2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	3.84
222		(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.10
223		2-[[[(2,3-Dimethyl-1H-indol-5-yl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.32
224		2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.03

225		2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.01
226		2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.37

Example 227

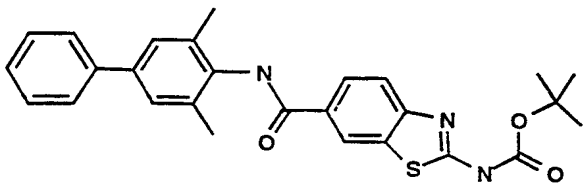
Preparation of 2-[[[[(1-methoxycarbonyl)cyclopropyl]amino]carbonyl]amino-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of the compounds of Table 1 using 1-methoxycarbonyl-cyclopropyl amine gave the title compound of this Example (6%) after purification by preparative HPLC under the following conditions: YMC ODS 20 x 100 mm Column, 10 min gradient starting from 70% solvent A (10% MeOH, 90% H_2O, 0.2% H_3PO_4) and 30% solvent B to 100% solvent B (90% MeOH, 10% H_2O, 0.2% H_3PO_4), flow rate 20 mL/min, λ = 220 nM. MS: 453 $(M+H)^+$.

Example 228

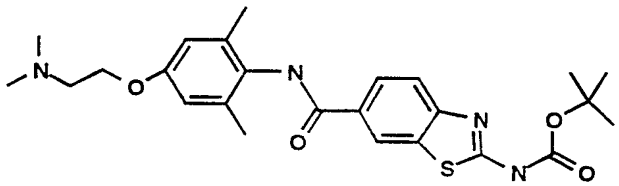
Preparation of [6-[[[(2,6-Dimethyl-4-phenyl)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



Analogous to the preparation of the compounds of Table 4 using 2,6-dimethyl-4-phenyl aniline gave the title compound of this Example (45%) after purification by silica gel chromatography and elution with 1-5% methanol in chloroform. MS: 474.1 $(M+H)^+$.

Example 229

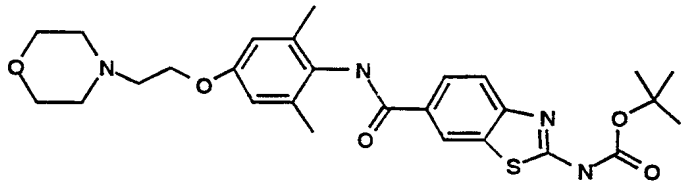
Preparation of [6-[[[(2,6-Dimethyl-4-(2-N,N-dimethylethoxy)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



Analogous to the preparation of the compounds of Table 4 using 2,6-dimethyl-4-(2-N,N-dimethylethoxy) aniline gave the title compound of this Example (45%) after purification by silica gel chromatography and elution with 2-5% methanol in chloroform and 95: 4: 1 chloroform: methanol: triethyl amine. MS: 485.1 $(M+H)^+$.

Example 230

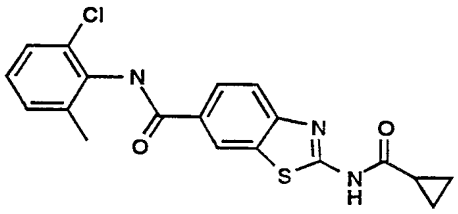
Preparation of [6-[[[(2,6-Dimethyl-4-(2-morpholinoethoxy)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester



Analogous to the preparation of the compounds of Table 4 using 2,6-dimethyl-4-(2-morpholinoethoxy) aniline gave the title compound of this Example (18%) after purification by silica gel chromatography and elution with 95: 4: 1 chloroform: methanol: triethyl amine. MS: 527.7 $(M+H)^+$.

Example 231

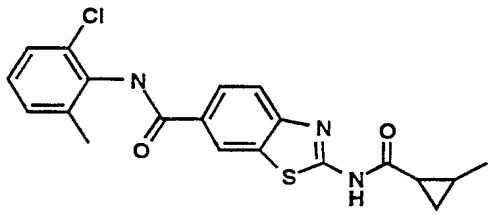
Preparation of 2-[(Cyclopropylcarbonyl)aminol-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **99** in Table 3 except using **166B(Alt)** afforded the title compound of this Example. MS: 386 $(M+H)^+$.

Example 232

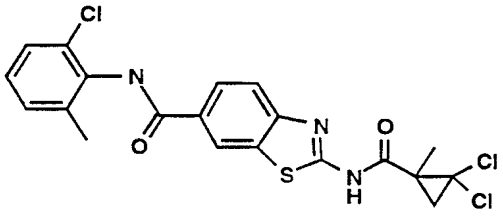
Preparation of 2-[(2-Methyl-cyclopropylcarbonyl)aminol-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **231** except using 2-methyl-cyclopropane carboxylic acid afforded the title compound of this Example. MS: 400 $(M+H)^+$.

Example 233

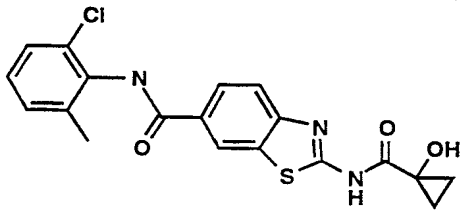
Preparation of 2-[(2,2-Dichloro-1-methyl-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **231** except using 2,2-dichloro-1-methyl-cyclopropane carboxylic acid afforded the title compound of this Example. MS: 469 $(M+H)^+$.

Example 234

Preparation of 2-[(1-Hydroxy-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide



Analogous to the preparation of **231** except using 1-hydroxy-cyclopropane carboxylic acid afforded the title compound of this Example. MS: 402 $(M+H)^+$.

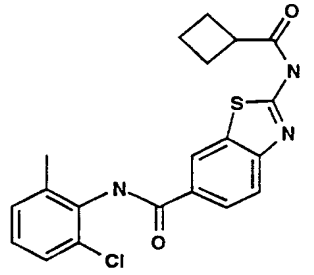
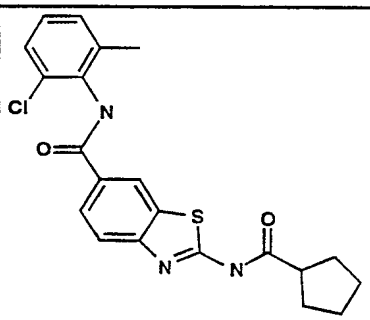
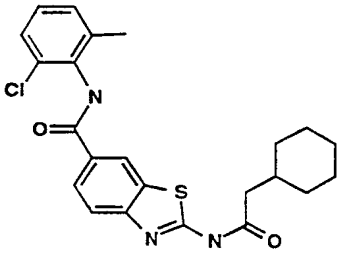
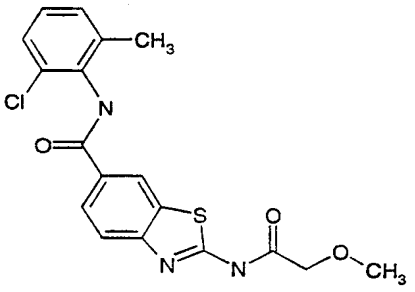
Examples 235 to 282 & 467 to 478

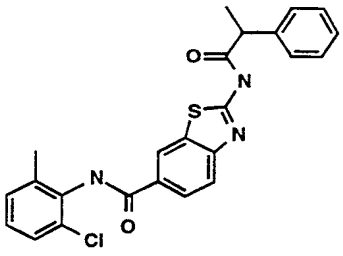
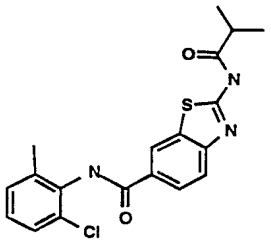
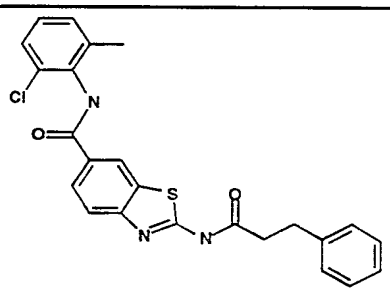
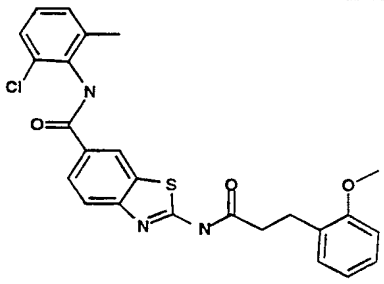
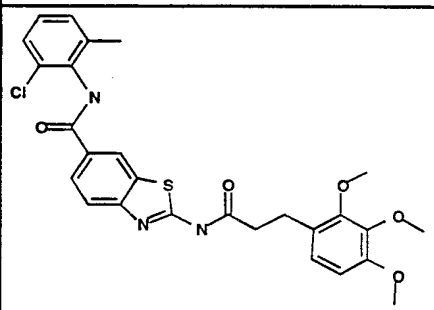
General Procedure

Compounds **235** to **282** and **467** to **478** were prepared following the procedure described below. Diisopropylethyl amine (50 µL, 0.288 mmol) was added to a mixture of compound **166B(Alt)** (30 mg, 0.096 mmol), carboxylic acid (0.115 mmol), 1-hydroxy-7-azabenzotriazole (17 mg, 0.125 mmol), and ethyl-3-(3-dimethylamino)-propyl carbodiimide hydrochloride (24 mg, 0.125 mmol) in THF (1 mL). The mixture was heated at 45°C for 18-72 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (2x), 1 N aq. NaOH solution (2x). The organic extract was dried ($MgSO_4$), filtered and concentrated in speedvac. The crude products were purified either by trituration with dichloromethane-ether or by automated preparative HPLC under the following conditions: YMC ODS 20 x 100 mm Column, 10 min gradient starting from 70% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) and 30% solvent B to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4), flow rate 20 mL/min, λ = 220 nM.

"HPLC Ret Time" is the HPLC retention time under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4) with 2 min hold, flow rate 4 mL/min, λ = 220 nM for compounds **235-271**, and and compounds

467-478, and Phenomenex-Prime S5, 4.6 x 50 mm Column, 2 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4) with 1 min hold, flow rate 5 mL/min, λ = 220 nM for compounds **272-282**.

EX. NO.	Compound Structure	Compound Name	HPLC Ret Time (min)
235		N-(2-Chloro-6-methylphenyl)-2-[(cyclobutylcarbonyl)amino]-6-benzothiazolecarboxamide	3.84
236		N-(2-Chloro-6-methylphenyl)-2-[(cyclopentylcarbonyl)amino]-6-benzothiazolecarboxamide	4.00
237		N-(2-Chloro-6-methylphenyl)-2-[(cyclohexylacetyl)amino]-6-benzothiazolecarboxamide	4.32
238		N-(2-Chloro-6-methylphenyl)-2-[(methoxyacetyl)amino]-6-benzothiazolecarboxamide	3.39

239		N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-2-phenylpropyl)amino]-6-benzothiazolecarboxamide	4.1
240		N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-2-methylpropyl)amino]-6-benzothiazolecarboxamide	4.06
241		N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-3-phenylpropyl)amino]-6-benzothiazolecarboxamide	4.11
242		N-(2-Chloro-6-methylphenyl)-2-[[3-(2-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide	4.16
243		N-(2-Chloro-6-methylphenyl)-2-[[1-oxo-3-(2,3,4-trimethoxyphenyl)propyl]amino]-6-benzothiazolecarboxamide	4.03

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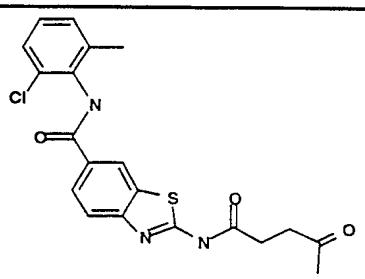
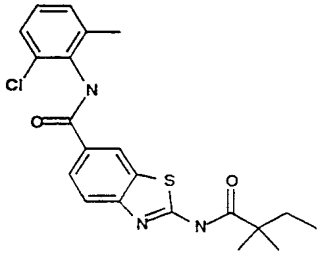
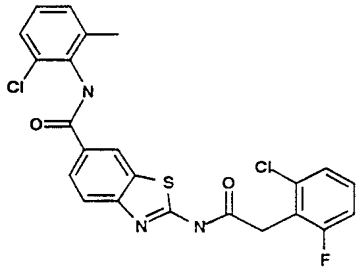
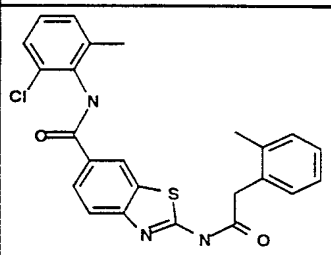
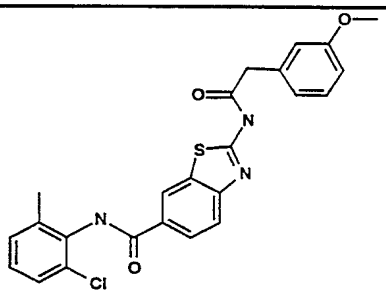
244		N-(2-Chloro-6-methylphenyl)-2-[(1,4-dioxopentyl)amino]-6-benzothiazolecarboxamide	3.37
245		N-(2-Chloro-6-methylphenyl)-2-[(2,2-dimethyl-1-oxobutyl)amino]-6-benzothiazolecarboxamide	4.04
246		2-[[(2-Chloro-6-fluorophenyl)acetyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.05
247		N-(2-Chloro-6-methylphenyl)-2-[[(2-methylphenyl)acetyl]amino]-6-benzothiazolecarboxamide	4.06
248		N-(2-Chloro-6-methylphenyl)-2-[[(3-methoxyphenyl)acetyl]amino]-6-benzothiazolecarboxamide	3.94

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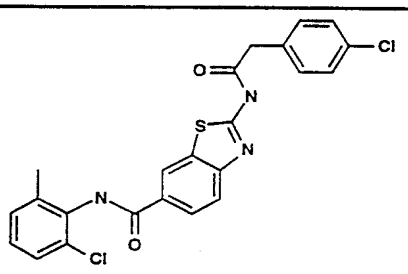
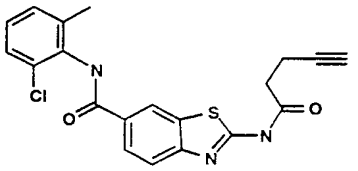
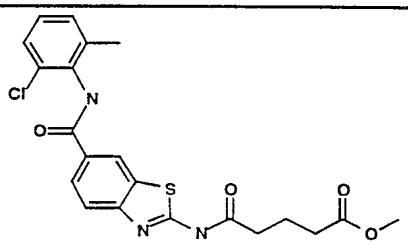
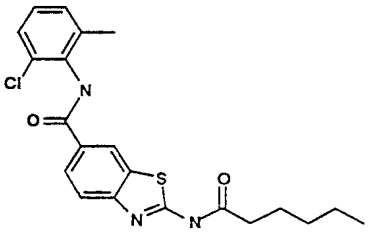
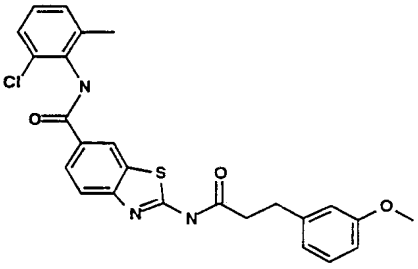
249		N-(2-Chloro-6-methylphenyl)-2-[[(4-chlorophenyl)acetyl]amino]-6-benzothiazolecarboxamide	4.19
250		N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-4-pentynyl)amino]-6-benzothiazolecarboxamide	3.58
251		5-[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]-5-oxopentanoic acid methyl ester	3.63
252		N-(2-Chloro-6-methylphenyl)-2-[(1-oxohexyl)amino]-6-benzothiazolecarboxamide	4.17
253		N-(2-Chloro-6-methylphenyl)-2-[[3-(3-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide	4.1

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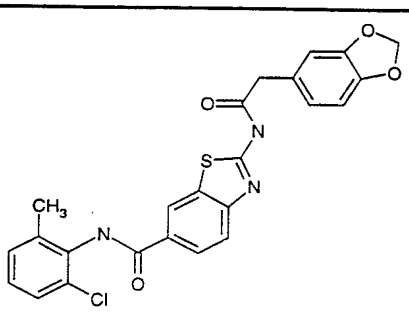
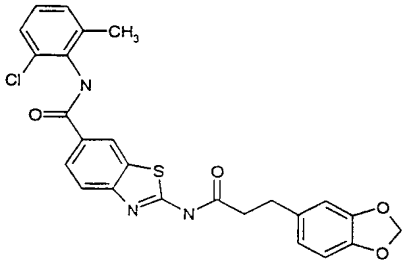
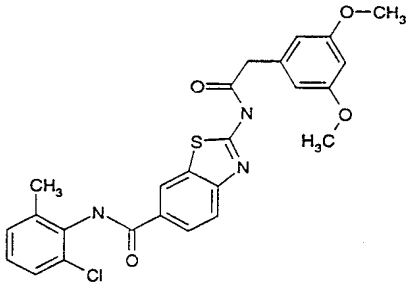
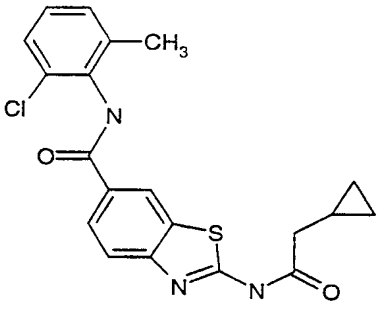
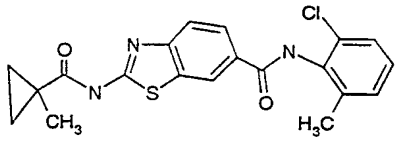
254		2-[[(1,3-Benzodioxol-5-yl)acetyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	3.89
255		2-[[3-(1,3-Benzodioxol-5-yl)-1-oxopropyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.08
256		N-(2-Chloro-6-methylphenyl)-2-[[(3,5-dimethoxyphenyl)acetyl]amino]-6-benzothiazolecarboxamide	3.95
257		N-(2-Chloro-6-methylphenyl)-2-[(cyclopropylacetyl)amino]-6-benzothiazolecarboxamide	3.76
258		N-(2-Chloro-6-methylphenyl)-2-[[(1-methylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	3.82

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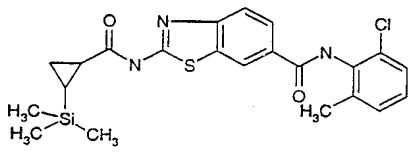
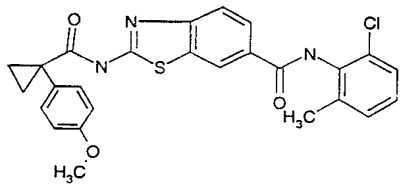
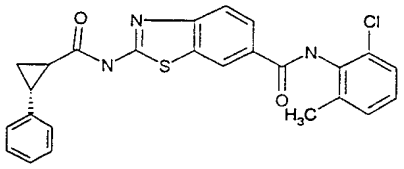
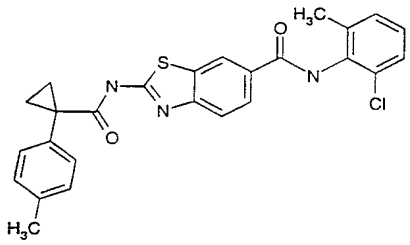
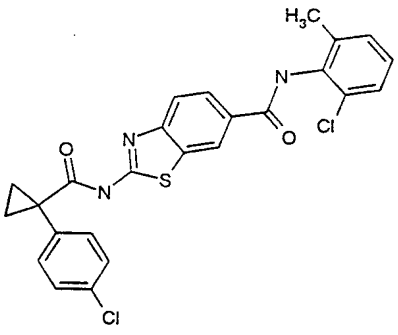
259		N-(2-Chloro-6-methylphenyl)-2-[[[2-(trimethylsilyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.55
260		N-(2-Chloro-6-methylphenyl)-2-[[[1-(4-methoxyphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.41
261		trans-N-(2-Chloro-6-methylphenyl)-2-[[(2-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	4.37
262		N-(2-Chloro-6-methylphenyl)-2-[[[1-(4-methylphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.51
263		N-(2-Chloro-6-methylphenyl)-2-[[[1-(4-chlorophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.49

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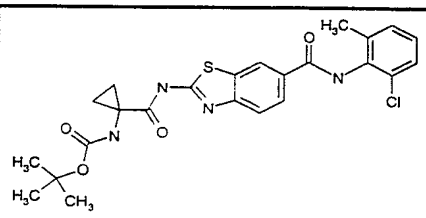
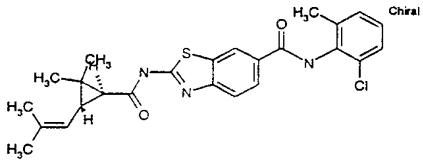
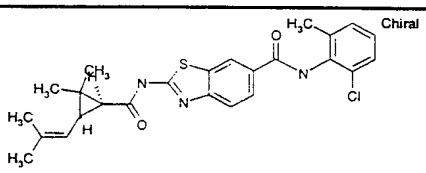
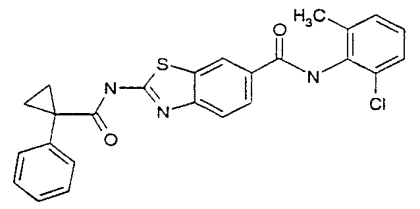
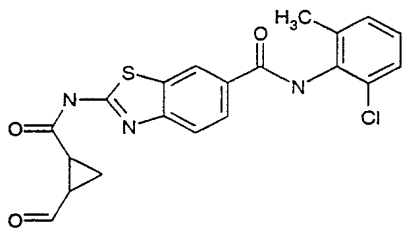
264		[1-[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropyl]carbamic acid 1,1-dimethylethyl ester	3.96
265		(1S-trans)-N-(2-Chloro-6-methylphenyl)-2-[[[2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.52
266		(1S-cis)-N-(2-Chloro-6-methylphenyl)-2-[[[2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.48
267		N-(2-Chloro-6-methylphenyl)-2-[[(1-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	4.30
268		N-(2-Chloro-6-methylphenyl)-2-[[(2-formylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	4.28

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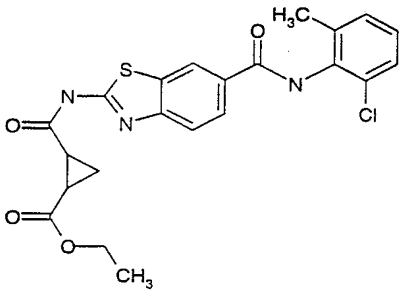
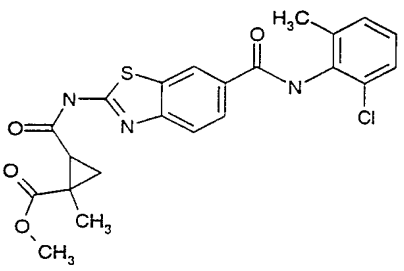
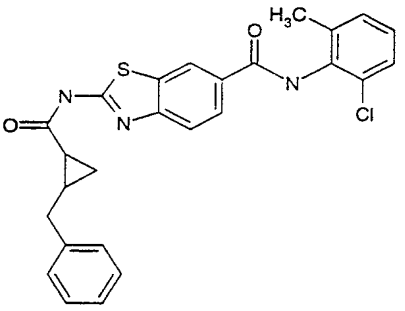
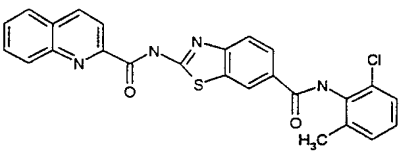
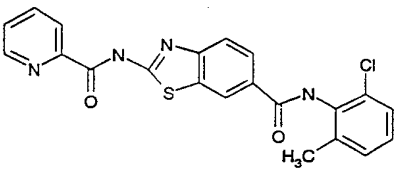
269		2-[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropanecarboxylic acid ethyl ester	4.04
270		2-[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]-1-methylcyclopropanecarboxylic acid methyl ester	3.95 3.98
271		N-(2-Chloro-6-methylphenyl)-2-[[[2-(phenylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.36
272		N-[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]-2-quinolinecarbox-amide	2.39
273		N-(2-Chloro-6-methylphenyl)-2-[(2-pyridinylcarbonyl)amino]-6-benzothiazolecarboxamide	2.14

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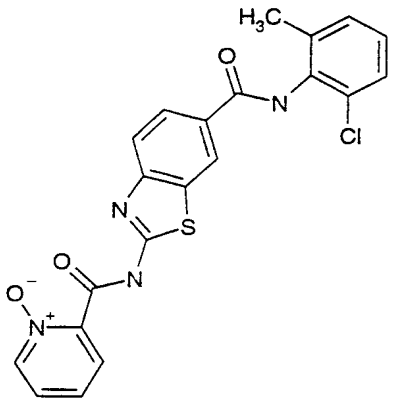
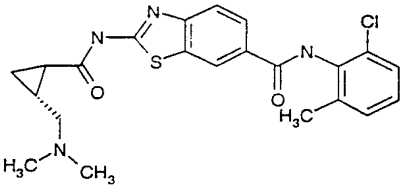
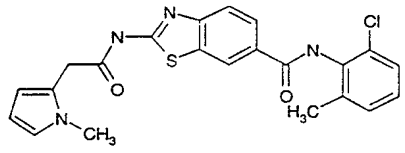
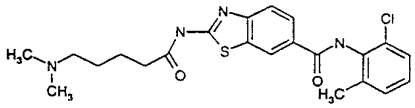
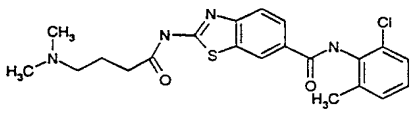
274		N-(2-Chloro-6-methylphenyl)-2-[(2-pyridinylcarbonyl)amino]-6-benzothiazolecarboxamide, 1-oxide	2.02
275		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[(dimethylamino)methyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	1.66
276		N-(2-Chloro-6-methylphenyl)-2-[[(1-methyl-1H-pyrrol-2-yl)acetyl]amino]-6-benzothiazolecarboxamide	2.07
277		N-(2-Chloro-6-methylphenyl)-2-[[5-(dimethylamino)-1-oxopentyl]amino]-6-benzothiazolecarboxamide	1.65
278		N-(2-Chloro-6-methylphenyl)-2-[[4-(dimethylamino)-1-oxobutyl]amino]-6-benzothiazolecarboxamide	1.58

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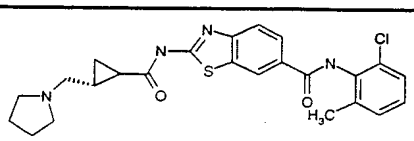
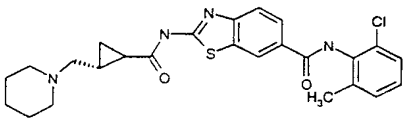
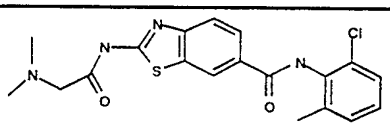
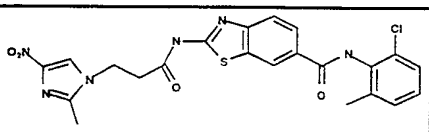
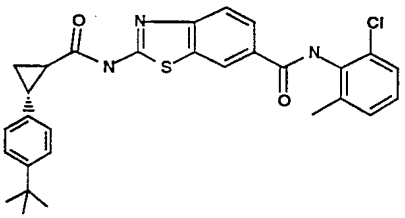
279		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(1-pyrrolidinylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	1.67
280		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(1-piperidinylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	1.70
281		N-(2-Chloro-6-methylphenyl)-2-[[(dimethylamino)acetyl]amino]-6-benzothiazolecarboxamide	1.49
282		N-(2-Chloro-6-methylphenyl)-2-[[3-(2-methyl-4-nitro-1H-imidazol-1-yl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide	1.91
467		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[4-(1,1-dimethylethyl)phenyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.87

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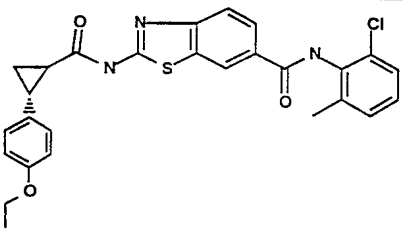
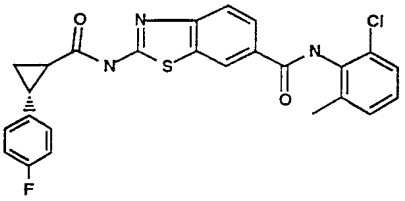
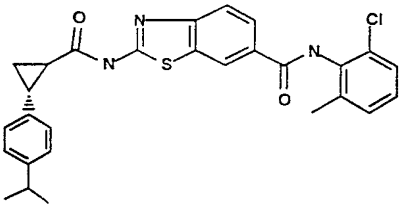
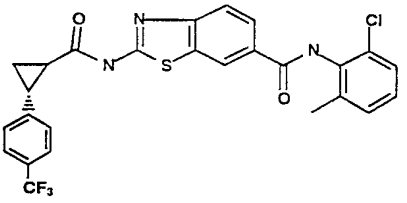
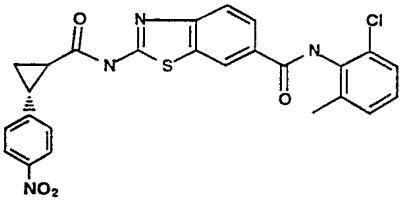
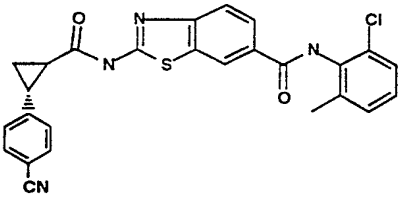
468		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-ethoxyphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.51
469		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-fluorophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.39
470		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[4-(1-methylethyl)phenyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.77
471		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[4-(trifluoromethyl)phenyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.57
472		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-nitrophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.36
473		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-cyanophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.20

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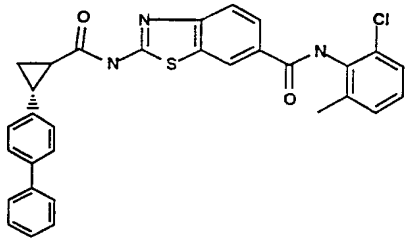
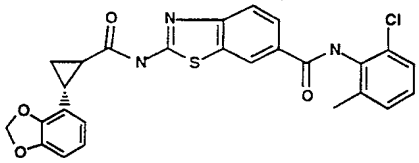
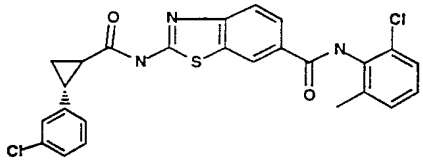
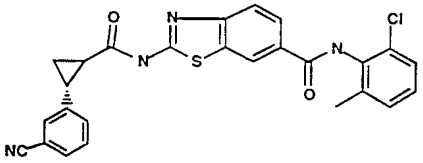
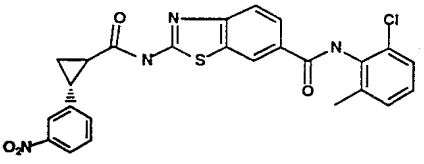
474		trans-2-[[(2-[1,1'-Biphenyl]-4-ylcyclopropyl)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.80
475		trans-2-[[[2-(1,3-Benzodioxol-4-yl)cyclopropyl]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.37
476		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(3-chlorophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.59
477		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(3-cyanophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.21
478		trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(3-nitrophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.37

Examples 283 to 322

General Procedure

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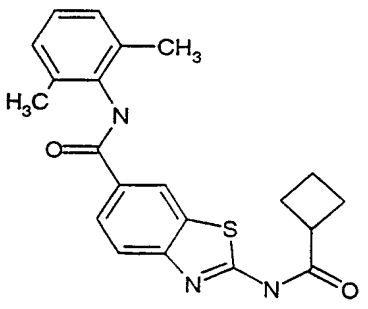
Compounds **283** to **322** were prepared following the procedure described below. Diisopropylethyl amine (50 μL, 0.288 mmol) was added to a mixture of compound **183B(Alt)** (30 mg, 0.096 mmol), carboxylic acid (0.115 mmol), 1-hydroxy-7-azabenzotriazole (17 mg, 0.125 mmol), and ethyl-3-(3-dimethylamino)-propyl carbodiimide hydrochloride (24 mg, 0.125 mmol) in THF (1 mL). The mixture was heated at 45°C for 18-72 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (2x), 1 N aq. NaOH solution (2x). The organic extract was dried ($MgSO_4$), filtered and concentrated in speedvac. The crude products were purified either by trituration with dichloromethane-ether or by automated preparative HPLC under the following conditions: YMC ODS 20 x 100 mm Column, 10 min gradient starting from 70% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) and 30% solvent B to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4), flow rate 20 mL/min, λ = 220 nM.

"HPLC Ret Time" is the HPLC retention time under the following conditions: YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4) with 2 min hold, flow rate 4 mL/min, λ = 220 nM.

EX. NO.	Compound Structure	Compound Name	HPLC Ret Time (min)
283		2-[(Cyclobutylcarbonyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.86

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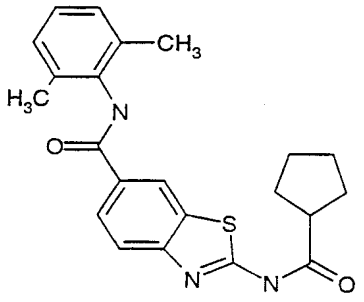
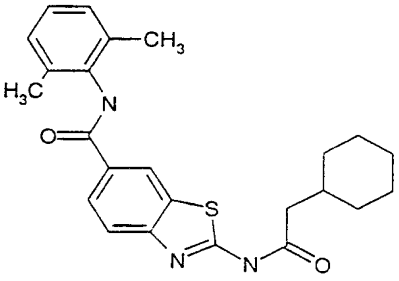
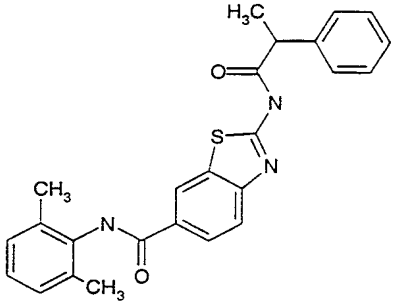
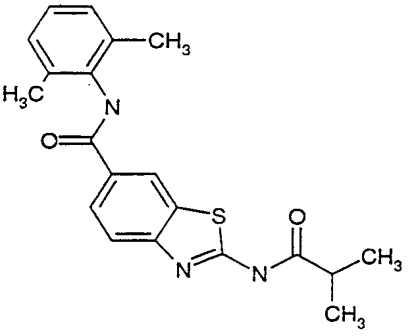
284		2-[(Cyclopentylcarbonyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.01
285		2-[(Cyclohexylacetyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.45
286		N-(2,6-Dimethylphenyl)-2-[(1-oxo-2-phenylpropyl)amino]-6-benzothiazolecarboxamide	4.1
287		N-(2,6-Dimethylphenyl)-2-[(2-methyl-1-oxopropyl)amino]-6-benzothiazolecarboxamide	3.73

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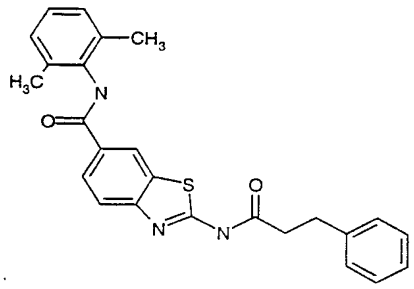
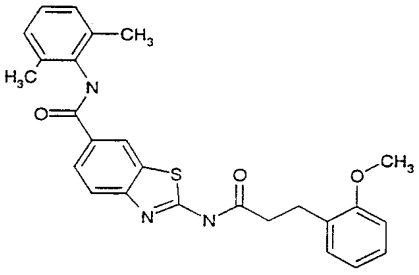
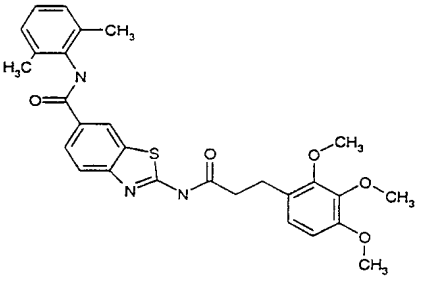
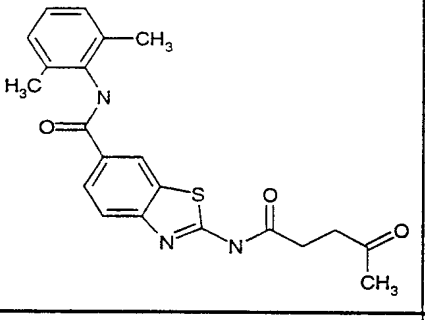
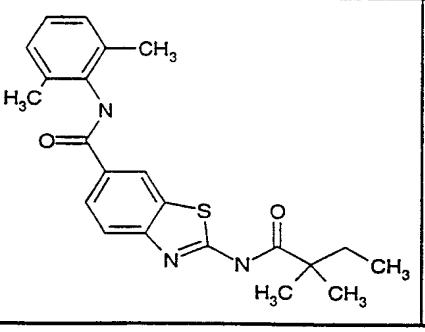
288		N-(2,6-Dimethylphenyl)-2-[(1-oxo-3-phenylpropyl)amino]-6-benzothiazolecarboxamide	4.11
289		N-(2,6-Dimethylphenyl)-2-[[3-(2-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide	4.15
290		N-(2,6-Dimethylphenyl)-2-[[3-(2,3,4-trimethoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide	4.00
291		N-(2,6-Dimethylphenyl)-2-[(1,4-dioxopentyl)amino]-6-benzothiazolecarboxamide	3.37
292		2-[(2,2-Dimethyl-1-oxobutyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.05

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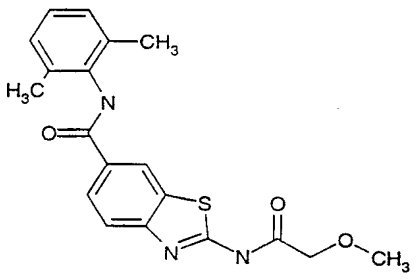
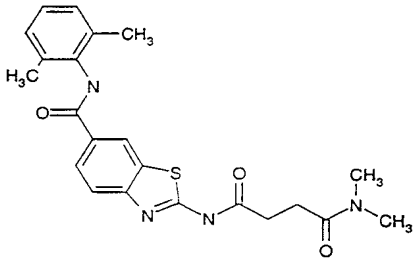
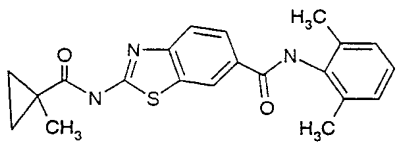
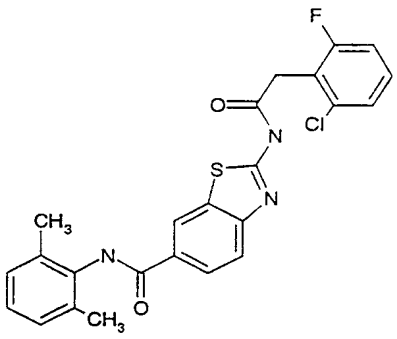
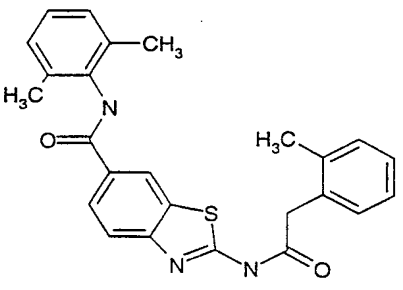
293		N-(2,6-Dimethylphenyl)-2-[(methoxyacetyl)amino]-6-benzothiazolecarboxamide	3.39
294		N,N-Dimethyl-N'-[6-[[(2,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]butanediamide	3.34
295		N-(2,6-Dimethylphenyl)-2-[[(1-methylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	3.83
296		2-[[(2-Chloro-6-fluorophenyl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.03
297		N-(2,6-Dimethylphenyl)-2-[[(2-methylphenyl)acetyl]amino]-6-benzothiazolecarboxamide	4.07

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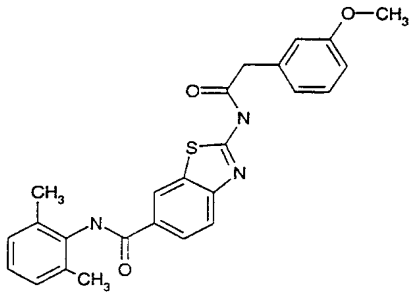
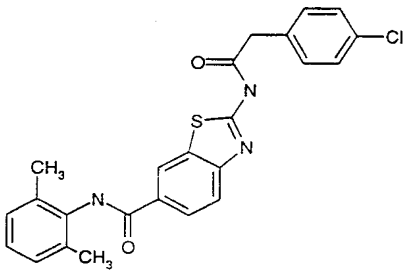
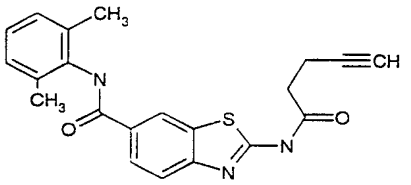
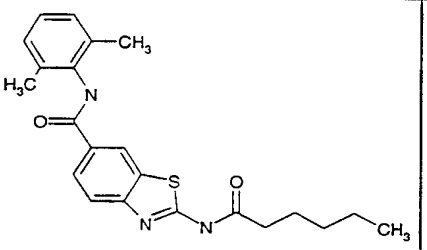
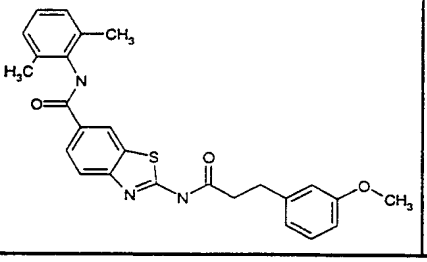
298		N-(2,6-Dimethylphenyl)-2-[[(3-methoxyphenyl)acetyl]amino]-6-benzothiazolecarboxamide	3.94
299		2-[[(4-Chlorophenyl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.19
300		N-(2,6-Dimethylphenyl)-2-[(1-oxo-4-pentynyl)amino]-6-benzothiazolecarboxamide	3.58
301		N-(2,6-Dimethylphenyl)-2-[(1-oxohexyl)amino]-6-benzothiazolecarboxamide	4.18
302		N-(2,6-Dimethylphenyl)-2-[[3-(3-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide	4.11

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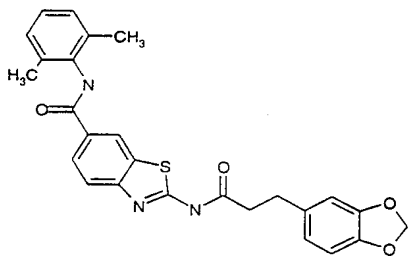
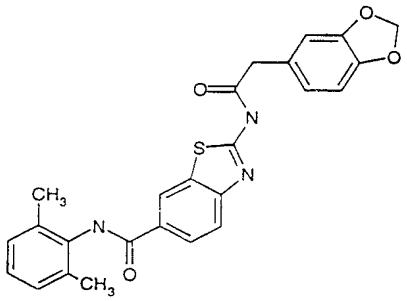
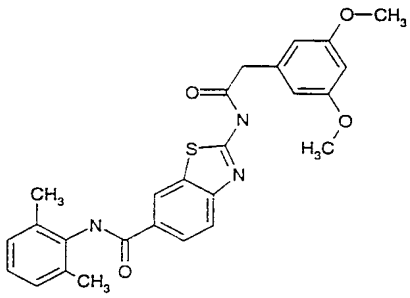
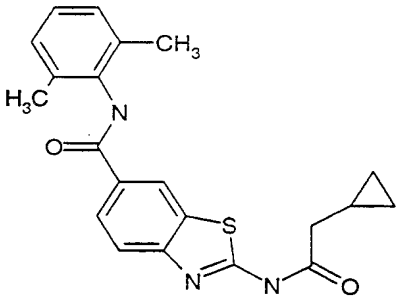
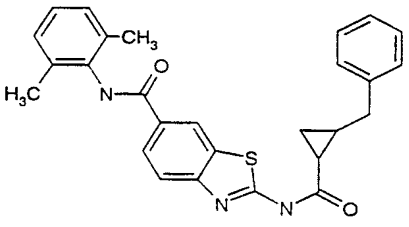
303		2-[[3-(1,3-Benzodioxol-5-yl)-1-oxopropyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.09
304		2-[[(1,3-Benzodioxol-5-yl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.91
305		2-[[(3,5-Dimethoxyphenyl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.97
306		2-[(Cyclopropylacetyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.79
307		N-(2,6-Dimethylphenyl)-2-[[[2-(phenylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.48

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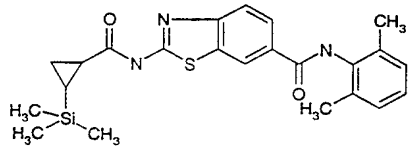
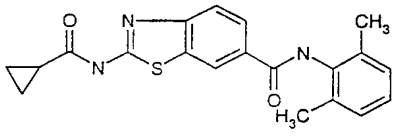
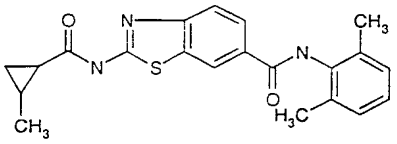
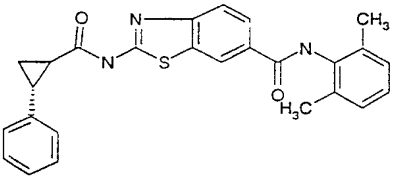
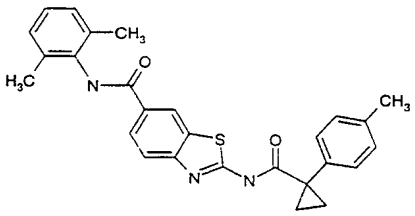
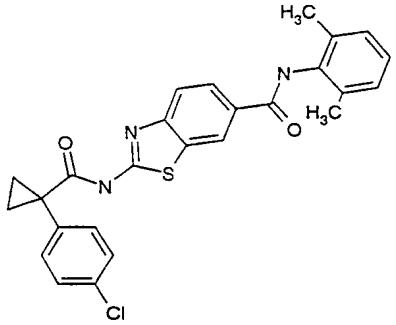
308		N-(2,6-Dimethylphenyl)-2-[[[2-(trimethylsilyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.58
309		2-[(Cyclopropylcarbonyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	3.82
310		N-(2,6-Dimethylphenyl)-2-[[(2-methylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	4.02
311		trans-N-(2,6-Dimethylphenyl)-2-[[(2-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	4.38
312		N-(2,6-Dimethylphenyl)-2-[[[1-(4-methylphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.50
313		2-[[[1-(4-Chlorophenyl)cyclopropyl]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.47

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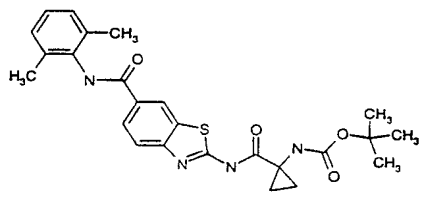
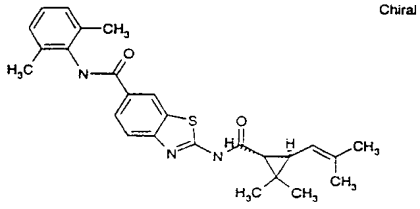
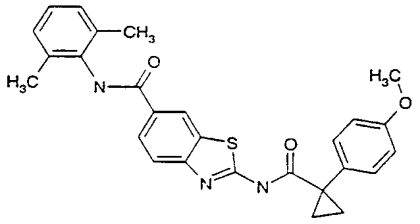
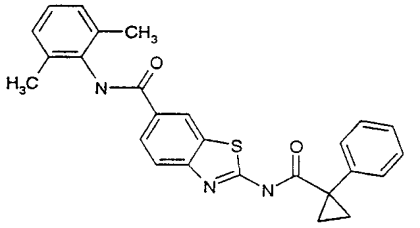
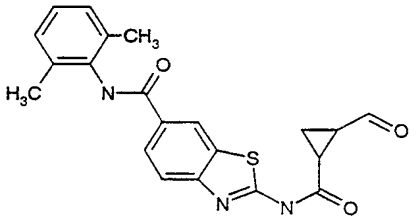
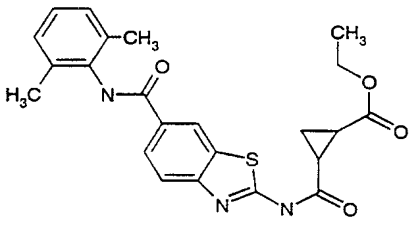
314		[1-[[[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropyl]carbamic acid 1,1-dimethylethyl ester	3.97
315	 Chiral	(1S-cis)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.50
316		N-(2,6-Dimethylphenyl)-2-[[[1-(4-methoxyphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.36
317		N-(2,6-Dimethylphenyl)-2-[[(1-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	4.32
318		N-(2,6-Dimethylphenyl)-2-[[(2-formylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide	4.29
319		2-[[[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropanecarboxylic acid ethyl ester	4.03

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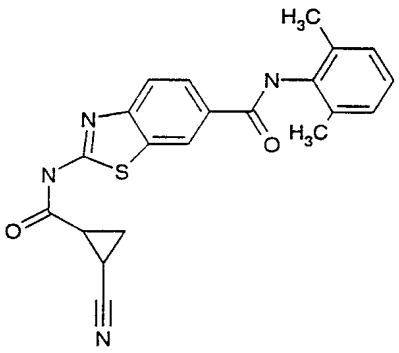
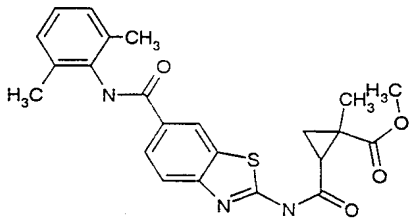
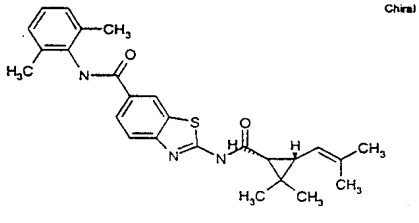
320		2-[[(2-Cyanocyclopropyl)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	2.5
321		2-[[[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]-1-methylcyclopropanecarboxylic acid methyl ester	3.97 4.00
322		(1S-trans)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide	4.53

Example 323 to 337

General Procedure

Compounds **323** to **337** were prepared following the procedure described below. Diisopropylethyl amine (50 µL, 0.288 mmol) was added to a mixture of the free base of compound **2** (30 mg, 0.096 mmol), carboxylic acid (0.115 mmol), 1-hydroxy-7-azabenzotriazole (17 mg, 0.125 mmol), and ethyl-3-(3-dimethylamino)-propyl carbodiimide hydrochloride (24 mg, 0.125 mmol) in THF (1 mL). The mixture was heated at 45°C for 18-72 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (2x), 1 N aq. NaOH solution (2x).

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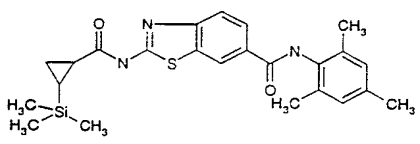
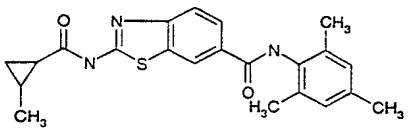
The organic extract was dried ($MgSO_4$), filtered and concentrated in speedvac. The crude products were purified either by trituration with dichloromethane-ether or by automated preparative HPLC under the following conditions: YMC ODS 20 x 100 mm Column, 10 min gradient starting from 70% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) and 30% solvent B to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4), flow rate 20 mL/min, λ = 220 nM.

"HPLC Ret Time" is the HPLC retention time under the following conditions: For compounds **327-334** the conditions are YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4) with 2 min hold, flow rate 4 mL/min, λ = 220 nM; for compounds **323-326** and **335-337** the conditions are YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.1% TFA) to 100% solvent B (90% MeOH, 10% H2O, 0.1% H3PO4) with 2 min hold, flow rate 4 mL/min, λ = 220 nM.

EX. NO.	Compound Structure	Compound Name	HPLC Ret Time (min)
323		N-(2,4,6-Trimethylphenyl)-2-[[[2-(trimethylsilyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide	4.70
324		2-[[(2-Methylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.18

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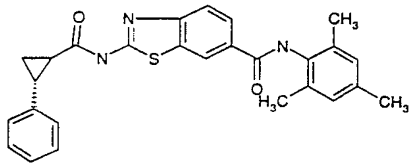
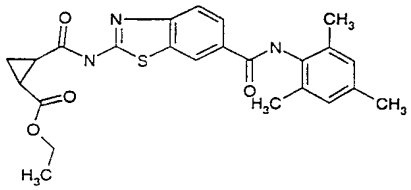
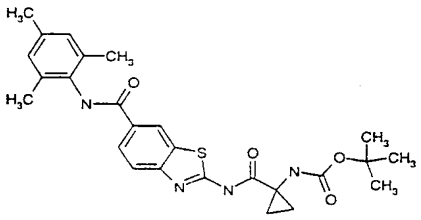
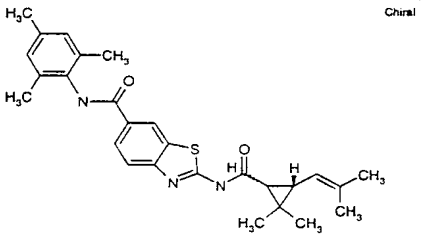
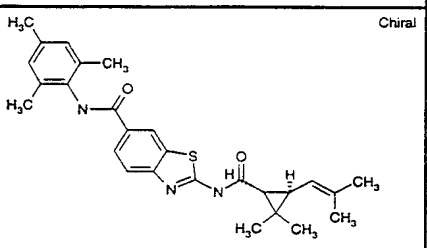
325		trans-2-[[(2-Phenylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.54
326		2-[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropanecarboxylic acid ethyl ester	4.32
327		[1-[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropyl]carbamic acid 1,1-dimethylethyl ester	4.15
328	 Chiral	(1S-trans)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.65
329	 Chiral	(1S-cis)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.63

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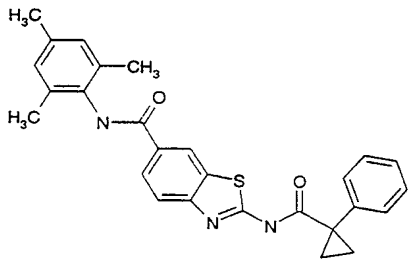
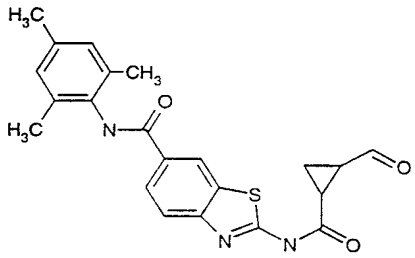
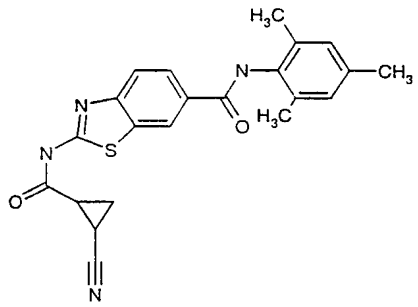
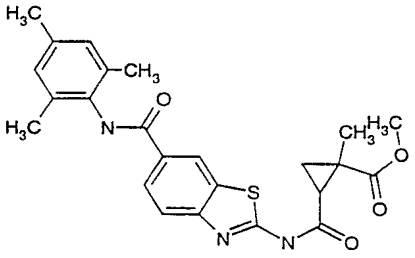
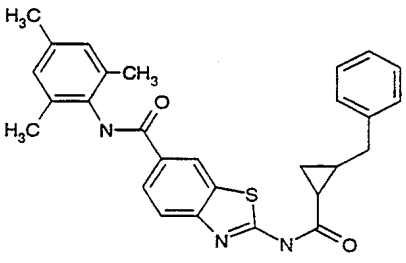
330		2-[[(1-Phenylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.45
331		2-[[(2-Formylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.43
332		2-[[(2-Cyanocyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.42
333		2-[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]-1-methylcyclopropanecarboxylic acid methyl ester	4.14
334		2-[[[2-(Phenylmethyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.48

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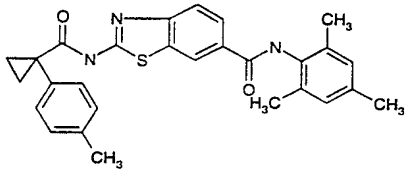
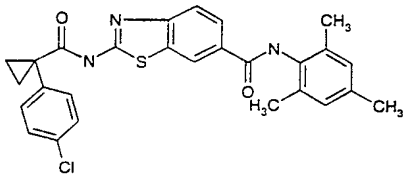
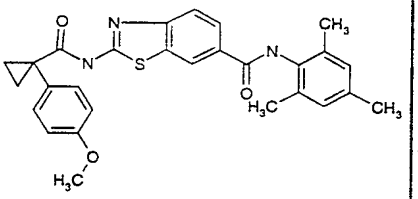
335		2-[[[1-(4-Methylphenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.73
336		2-[[[1-(4-Chlorophenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.68
337		2-[[[1-(4-Methoxyphenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide	4.59

Example 338 to 466

General Procedure

Compounds **338** to **466** were prepared following the procedure described below. Appropriate amine (0.086 mmol) was added to a solution of **166A** (30 mg, 0.072 mmol) in THF (3 mL). The solution was stirred at 57°C for 48-72 h. The reaction mixture was diluted with dichloromethane (5 mL) and washed with 1 N aq. HCl solution (2x), 1 N aq. NaOH solution (2x). The organic extract was dried (Na_2SO_4), filtered and concentrated in vacuo to obtain the titled compounds. Some of the analogs required purification by automated preparative HPLC under the following conditions: YMC ODS 20 x 100 mm Column, 10 min gradient starting from 70% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) and 30% solvent B to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4), flow rate 20 mL/min, λ = 220 nM.

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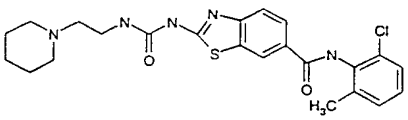
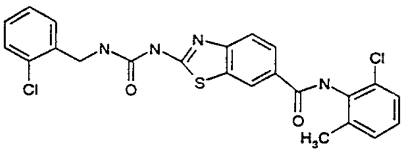
"HPLC Ret Time" is the HPLC retention time under the following conditions: Phenomenex-Prime S5 C18 4.6 x 30 mm, 2 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4) with 1 min hold, flow rate 5 mL/min, λ = 220 nM for compounds **387-388**; **390-405**; **422**; **426-428**; **431-466**; Phenomenex-LUNA S5 C18 4.6 x 30 mm, 2 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.1% TFA) to 100% solvent B (90% MeOH, 10% H2O, 0.1% TFA) with 1 min hold, flow rate 5 mL/min, λ = 220 nM for compounds **338-340**; **344-345**; **347-386**; **389**; **406-421**; **423-425**; **429-430**; and YMC S5 ODS 4.6 x 50 mm Ballastic Column, 4 min gradient starting from 100% solvent A (10% MeOH, 90% H2O, 0.2% H3PO4) to 100% solvent B (90% MeOH, 10% H2O, 0.2% H3PO4) with 2 min hold, flow rate 4 mL/min, λ = 220 nM for compounds **341-343**; and **346**.

EX. NO.	Compound Structure	Compound Name	HPLC Ret Time (min)
338		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-piperidinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.76
339		N-(2-Chloro-6-methylphenyl)-2-[[[[(2-chlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.55

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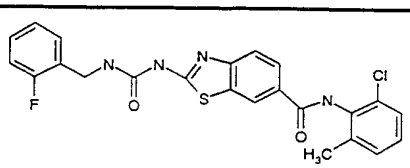
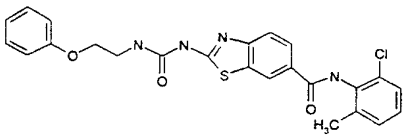
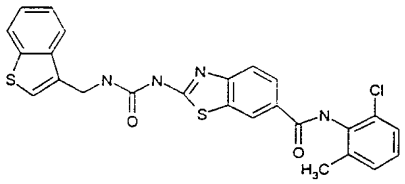
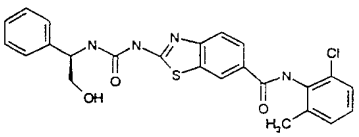
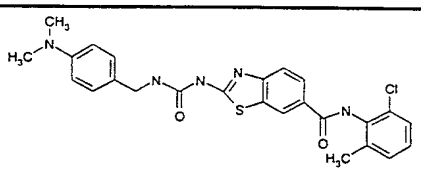
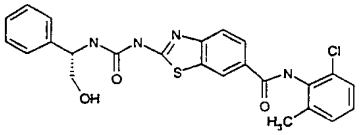
340		N-(2-Chloro-6-methylphenyl)-2-[[[[(2-fluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.23
341		N-(2-Chloro-6-methylphenyl)-2-[[[(2-phenoxyethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	4.16
342		2-[[[(Benzo[b]thiophen-3-ylmethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	4.31
343	Chiral 	(R)-N-(2-Chloro-6-methylphenyl)-2-[[[(2-hydroxy-1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	3.82
344		N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(dimethylamino)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.81
345	Chiral 	(S)-N-(2-Chloro-6-methylphenyl)-2-[[[(2-hydroxy-1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.13

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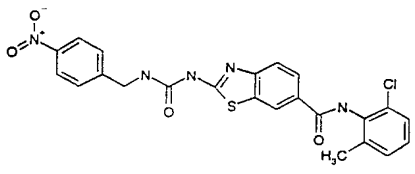
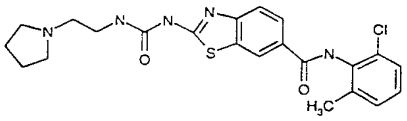
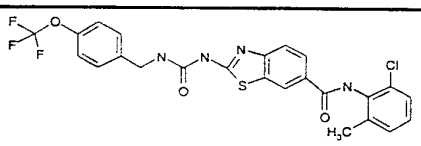
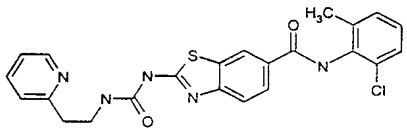
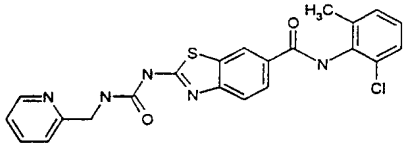
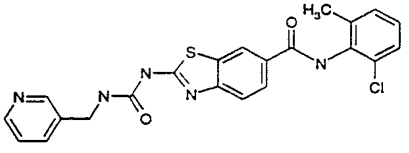
346		N-(2-Chloro-6-methylphenyl)-2-[[[[(4-nitrophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	3.96
347		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-pyrrolidinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.73
348		N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.38
349		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.61
350		N-(2-Chloro-6-methylphenyl)-2-[[[(2-pyridinylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.62
351		N-(2-Chloro-6-methylphenyl)-2-[[[(3-pyridinylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.59

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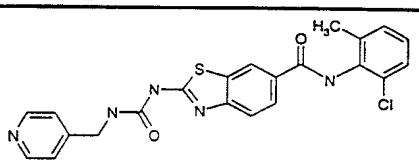
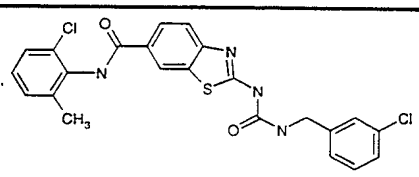
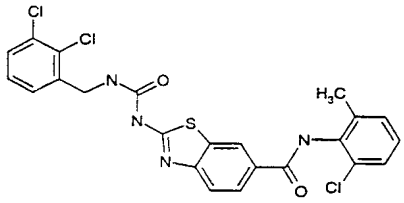
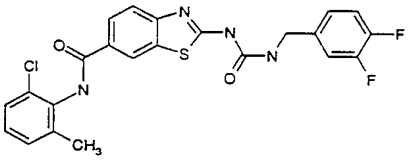
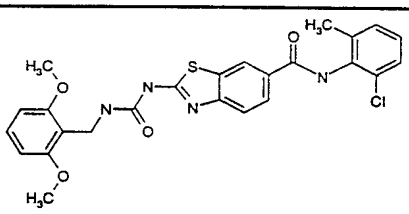
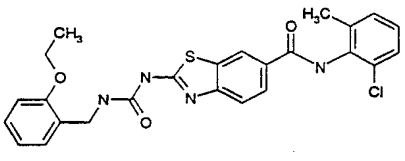
352		N-(2-Chloro-6-methylphenyl)-2-[[[(4-pyridinylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.58
353		N-(2-Chloro-6-methylphenyl)-2-[[[[(3-chlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.27
354		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,3-dichlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.35
355		N-(2-Chloro-6-methylphenyl)-2-[[[[(3,4-difluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.22
356		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,6-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.24
357		N-(2-Chloro-6-methylphenyl)-2-[[[[(2-ethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.29

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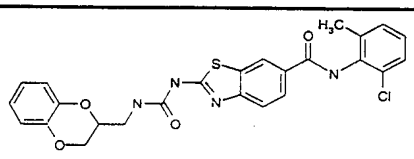
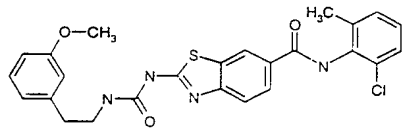
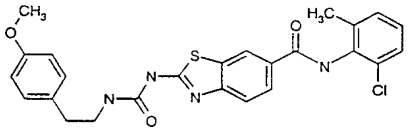
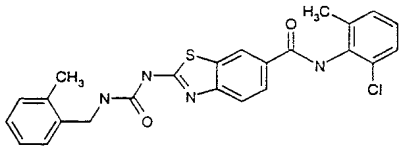
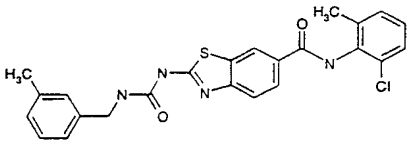
358		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,3-dihydro-1,4-benzodioxin-2-yl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.25
359		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(3-methoxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.23
360		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(4-methoxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.22
361		N-(2-Chloro-6-methylphenyl)-2-[[[[(2-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.24
362		N-(2-Chloro-6-methylphenyl)-2-[[[[(3-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.25

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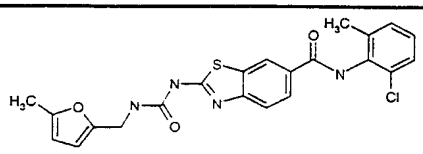
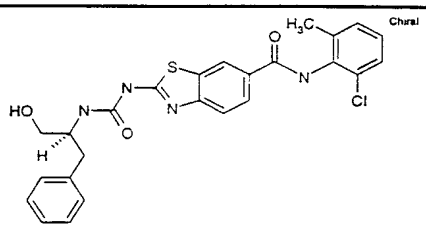
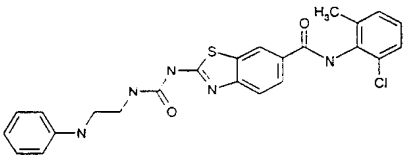
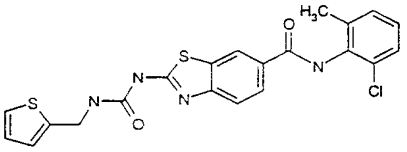
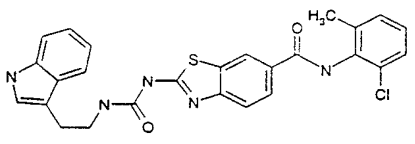
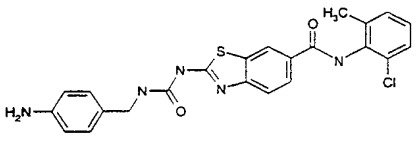
363		N-(2-Chloro-6-methylphenyl)-2-[[[[(5-methyl-2-furanyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.14
364		(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(hydroxymethyl)-2-phenylethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.13
365		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(phenylamino)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.96
366		N-(2-Chloro-6-methylphenyl)-2-[[[(2-thienylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.11
367		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1H-indol-3-yl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.19
368		2-[[[[(4-Aminophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	1.69

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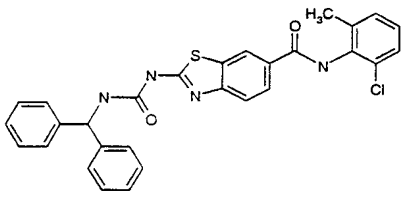
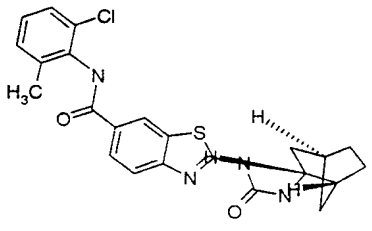
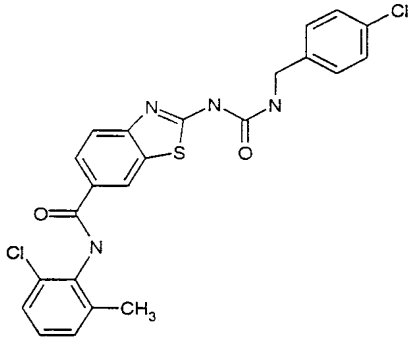
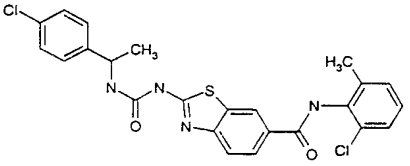
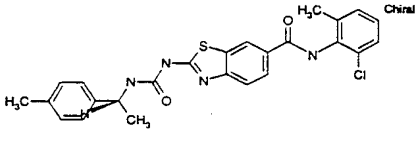
369		N-(2-Chloro-6-methylphenyl)-2-[[[(diphenylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.34
370	 Chiral	(1R-exo)-2-[[(Bicyclo[2.2.1]heptan-2-ylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.29
371		N-(2-Chloro-6-methylphenyl)-2-[[[[(4-chlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.26
372		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-chlorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.31
373	 Chiral	(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-methylphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.30

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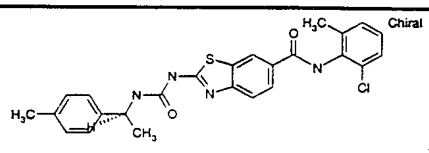
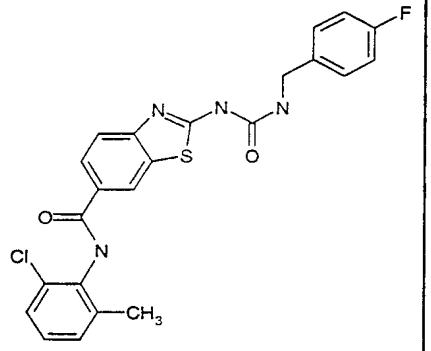
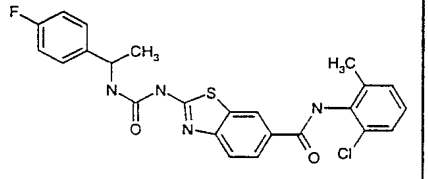
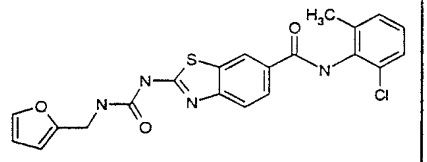
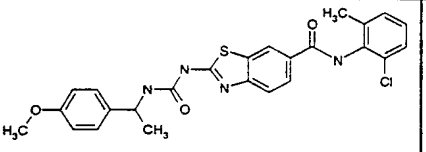
374		(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-methylphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.30
375		N-(2-Chloro-6-methylphenyl)-2-[[[[(4-fluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.17
376		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-fluorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.22
377		N-(2-Chloro-6-methylphenyl)-2-[[[(2-furanylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.05
378		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-methoxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.20

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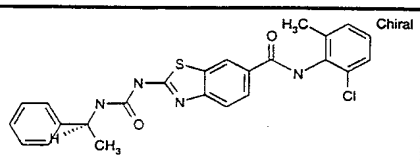
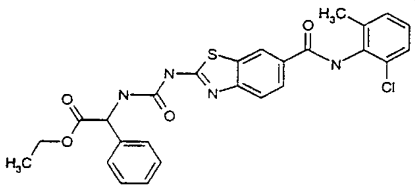
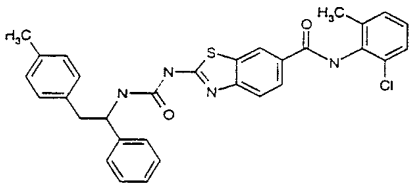
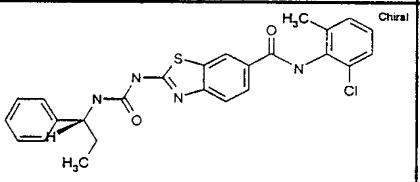
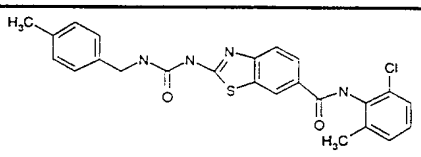
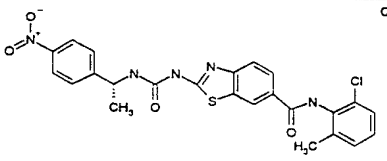
379	 Chiral	(S)-N-(2-Chloro-6-methylphenyl)-2-[[[(1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.20
380		α-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]benzeneacetic acid ethyl ester	2.22
381		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(4-methylphenyl)-1-phenylethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.44
382	 Chiral	(R)-N-(2-Chloro-6-methylphenyl)-2-[[[(1-phenylpropyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.27
383		N-(2-Chloro-6-methylphenyl)-2-[[[[(4-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.30
384	 Chiral	(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-nitrophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.26

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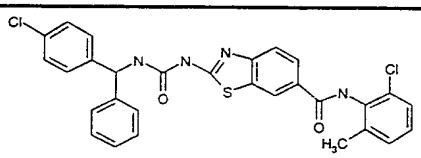
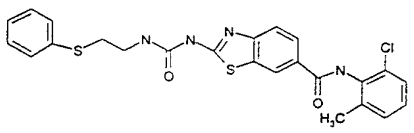
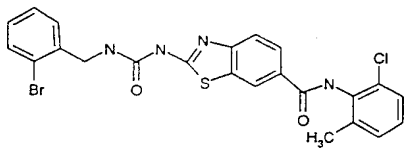
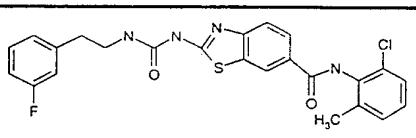
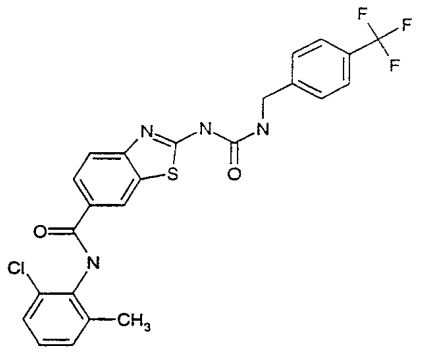
385		N-(2-Chloro-6-methylphenyl)-2-[[[[(4-chlorophenyl)phenylmethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.49
386		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(phenylthio)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.33
387		2-[[[[(2-Bromophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.26
388		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(3-fluorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.23
389		N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(trifluoromethyl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.28

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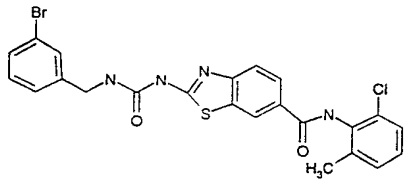
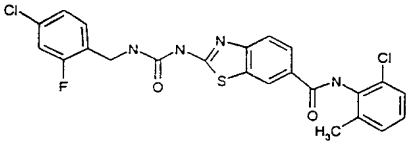
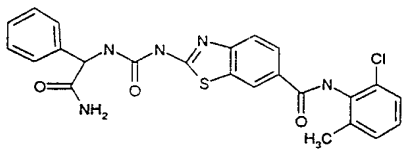
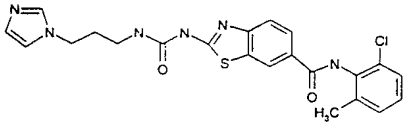
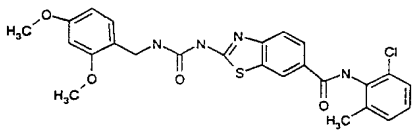
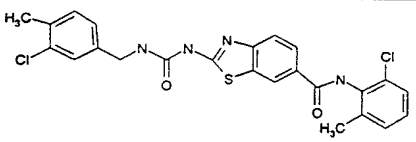
390		2-[[[[(3-Bromophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.28
391		2-[[[[(4-Chloro-2-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.28
392		2-[[[(2-Amino-2-oxo-1-phenylethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.36
393		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(1H-imidazol-1-yl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.61
394		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,4-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.19
395		N-(2-Chloro-6-methylphenyl)-2-[[[[(3-chloro-4-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.34

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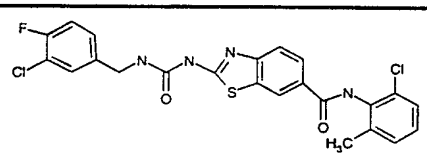
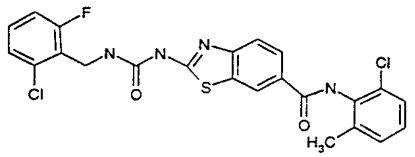
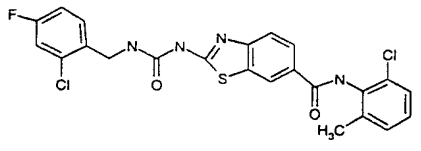
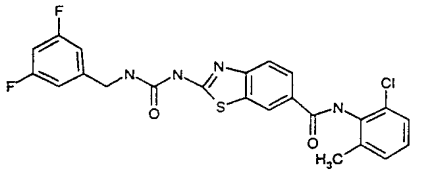
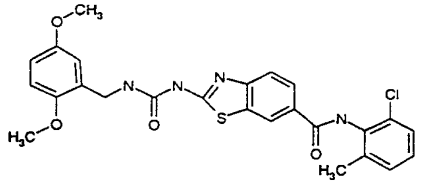
396		2-[[[[(3-Chloro-4-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.27
397		2-[[[[(2-Chloro-6-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.22
398		2-[[[[(2-Chloro-4-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.28
399		N-(2-Chloro-6-methylphenyl)-2-[[[[(3,5-difluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.20
400		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,5-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.18

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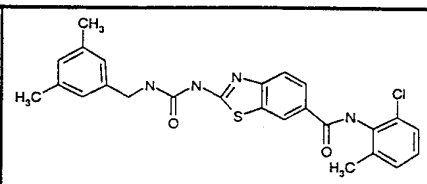
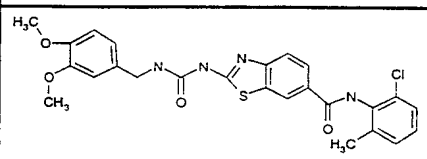
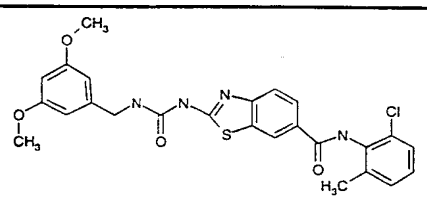
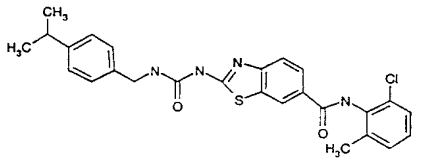
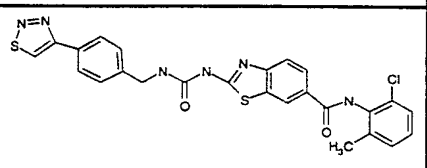
401		N-(2-Chloro-6-methylphenyl)-2-[[[[(3,5-dimethylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.32
402		N-(2-Chloro-6-methylphenyl)-2-[[[[(3,4-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.04
403		N-(2-Chloro-6-methylphenyl)-2-[[[[(3,5-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.15
404		N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(1-methylethyl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.38
405		N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.10

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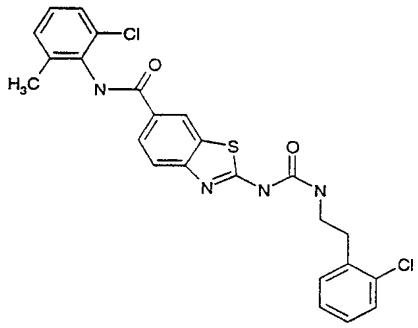
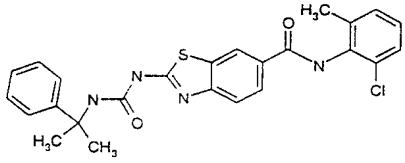
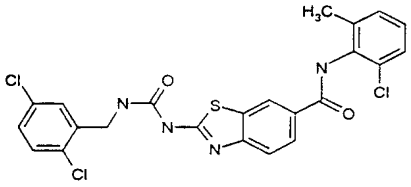
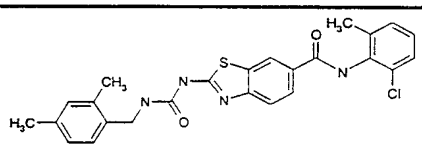
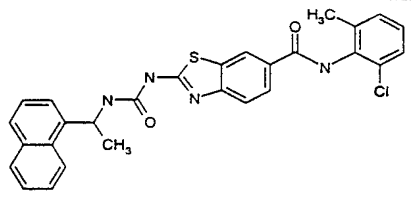
406		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(2-chlorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.29
407		N-(2-Chloro-6-methylphenyl)-2-[[[(1-methyl-1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.24
408		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,5-dichlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.34
409		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,4-dimethylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.32
410		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.34

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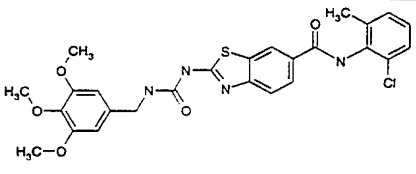
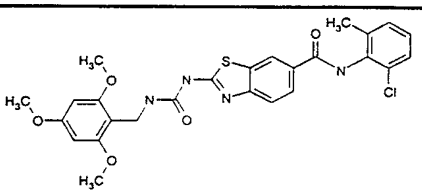
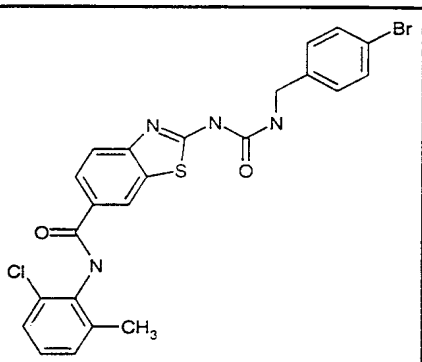
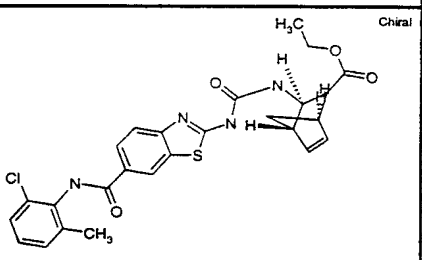
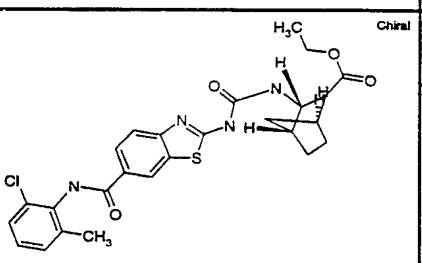
411		N-(2-Chloro-6-methylphenyl)-2-[[[[(3,4,5-trimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.06
412		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,4,6-trimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.22
413		2-[[[[(4-Bromophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.29
414		[1R-(endo,endo)]-3-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]bicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester	2.19
415		[1S-(exo,exo)]-3-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]bicyclo[2.2.1]heptane-2-carboxylic acid ethyl ester	2.25

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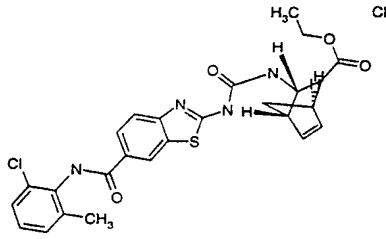
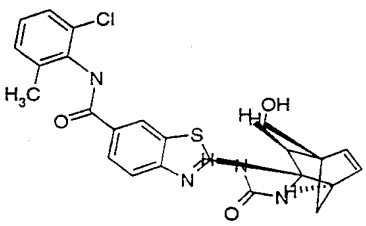
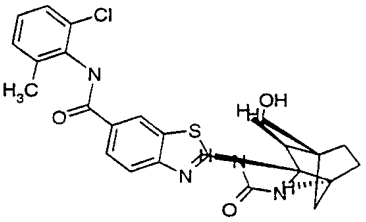
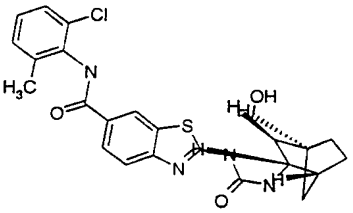
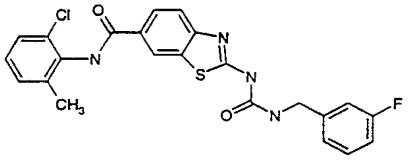
416	 Chiral	[1R-(exo,exo)]-3-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]bicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester	2.22
417	 Chiral	[1R-(endo,endo)]-N-(2-Chloro-6-methylphenyl)-2-[[[[3-(hydroxymethyl)bicyclo[2.2.1]hept-5-en-2-yl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.07
418	 Chiral	[1S-(endo,endo)]-N-(2-Chloro-6-methylphenyl)-2-[[[[3-(hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.11
419	 Chiral	[1R-(exo,exo)]-N-(2-Chloro-6-methylphenyl)-2-[[[[3-(hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.14
420		N-(2-Chloro-6-methylphenyl)-2-[[[[(3-fluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.17

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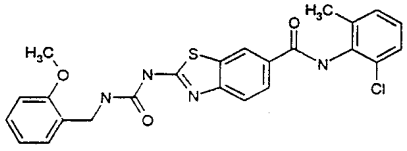
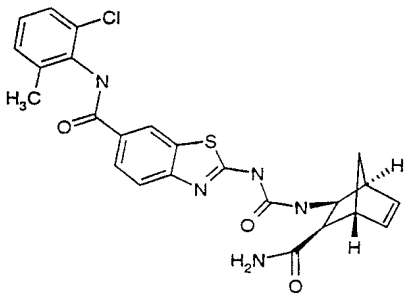
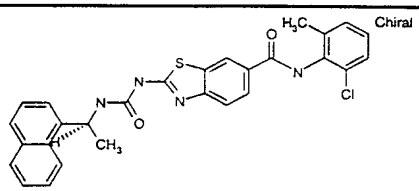
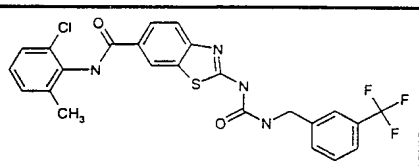
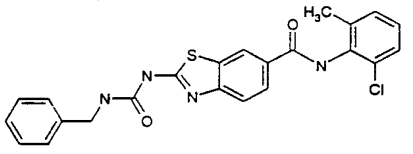
421		N-(2-Chloro-6-methylphenyl)-2-[[[[(2-methoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.19
422		(exo,exo)-2-[[[[3-(Aminocarbonyl)bicyclo[2.2.1]hept-5-en-2-yl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.07
423		(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.34
424		N-(2-Chloro-6-methylphenyl)-2-[[[[[3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.27
425		N-(2-Chloro-6-methylphenyl)-2-[[[(phenylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.15

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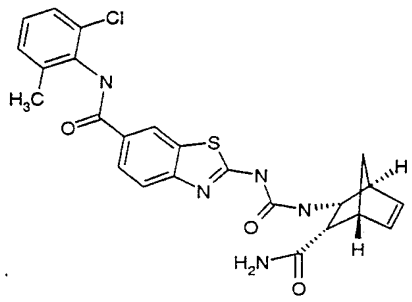
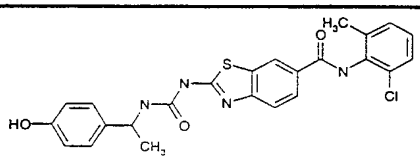
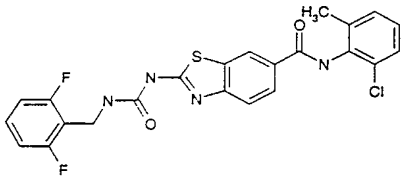
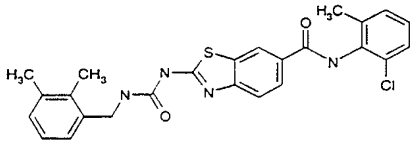
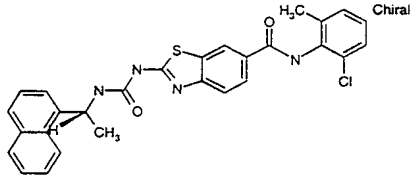
426		(endo,endo)-2-[[[[3-(Aminocarbonyl)bicyclo[2.2.1]hept-5-en-2-yl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.06
427		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-hydroxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.05
428		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,6-difluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.22
429		N-(2-Chloro-6-methylphenyl)-2-[[[[(2,3-dimethylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.30
430		(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.34

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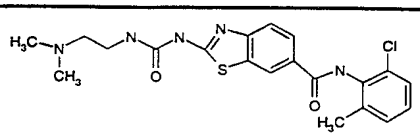
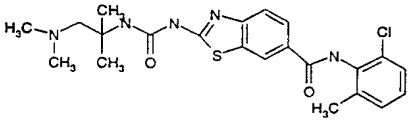
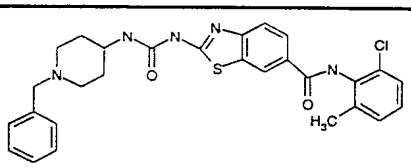
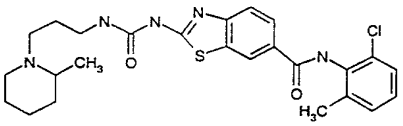
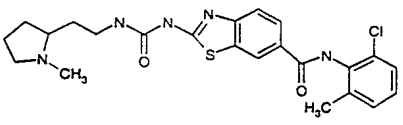
431		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(dimethylamino)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.70
432		N-(2-Chloro-6-methylphenyl)-2-[[[[1,1-dimethyl-2-(dimethylamino)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.71
433		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.62
434		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(2-methyl-1-piperidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.70
435		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.65

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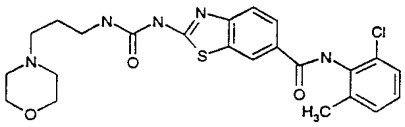
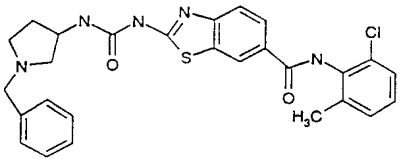
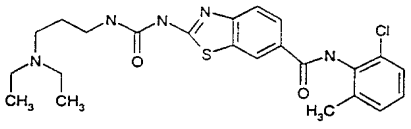
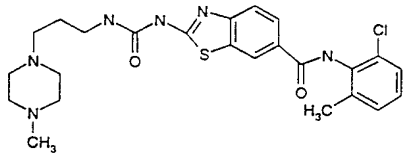
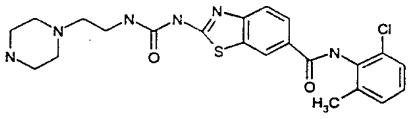
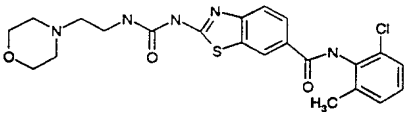
436		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(4-morpholinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.60
437		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.81
438		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(diethylamino)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.65
439		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(4-methyl-1-piperazinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.51
440		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-piperazinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.46
441		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(4-morpholinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.58

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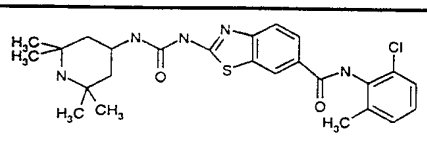
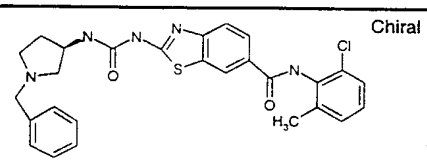
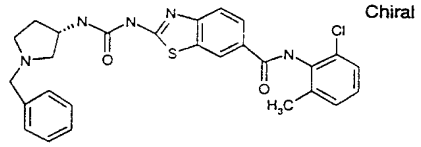
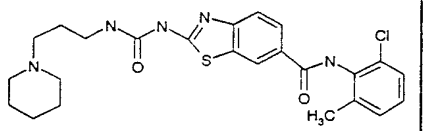
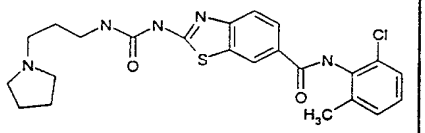
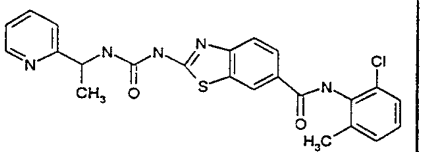
442		N-(2-Chloro-6-methylphenyl)-2-[[[(2,2,6,6-tetramethyl-4-piperidinyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.77
443	 Chiral	(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.80
444	 Chiral	(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.80
445		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(1-piperidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.65
446		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(1-pyrrolidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.62
447		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(2-pyridinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.70

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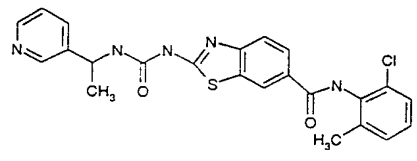
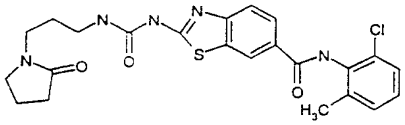
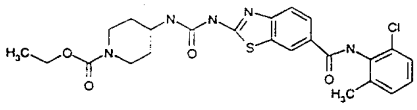
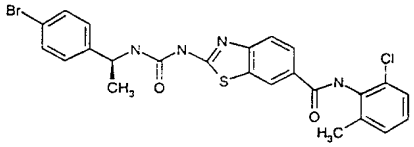
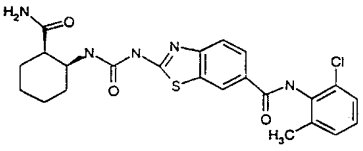
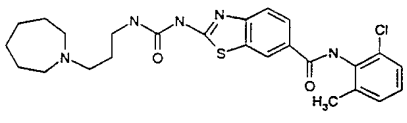
448		N-(2-Chloro-6-methylphenyl)-2-[[[[1-(3-pyridinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.65
449		N-(2-Chloro-6-methylphenyl)-2-[[[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.91
450		4-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]-1-piperidinecarboxylic acid ethyl ester	2.12
451		(S)-2-[[[[1-(4-Bromophenyl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.34
452	 Chiral	(1S-cis)-2-[[[[2-(Aminocarbonyl)cyclohexyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	2.02
453		2-[[[[3-(1H-Azepin-1-yl)propyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide	1.70

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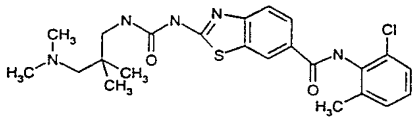
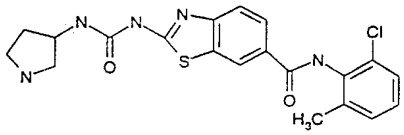
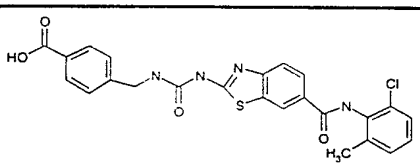
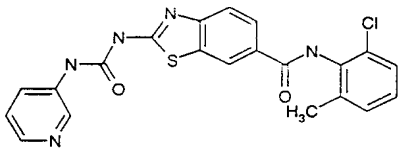
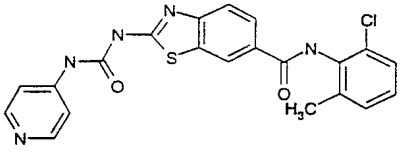
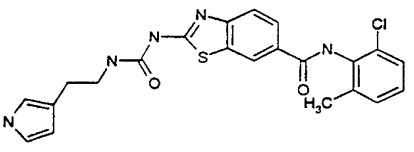
454		N-(2-Chloro-6-methylphenyl)-2-[[[[2,2-dimethyl-3-(dimethylamino)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.65
455		N-(2-Chloro-6-methylphenyl)-2-[[(3-pyrrolidinylamino)carbonyl]amino]-6-benzothiazolecarboxamide	1.54
456		4-[[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]methyl]benzoic acid	2.02
457		N-(2-Chloro-6-methylphenyl)-2-[[(3-pyridinylamino)carbonyl]amino]-6-benzothiazolecarboxamide	1.74
458		N-(2-Chloro-6-methylphenyl)-2-[[(4-pyridinylamino)carbonyl]amino]-6-benzothiazolecarboxamide	1.73
459		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1H-pyrrol-3-yl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.75

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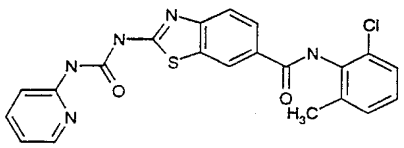
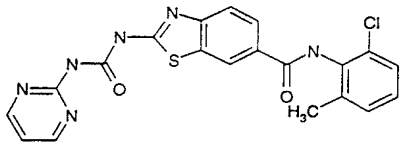
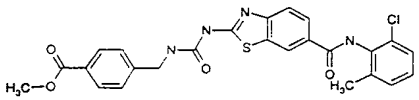
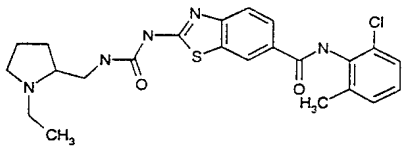
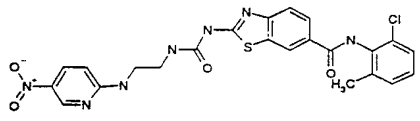
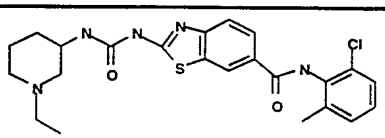
460		N-(2-Chloro-6-methylphenyl)-2-[[(2-pyridinylamino)carbonyl]amino]-6-benzothiazolecarboxamide	2.06
461		N-(2-Chloro-6-methylphenyl)-2-[[(2-pyrimidinylamino)carbonyl]amino]-6-benzothiazolecarboxamide	2.03
462		4-[[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]methyl]benzoic acid methyl ester	2.14
463		N-(2-Chloro-6-methylphenyl)-2-[[[[(1-ethyl-2-pyrrolidinyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.63
464		N-(2-Chloro-6-methylphenyl)-2-[[[[2-[(5-nitro-2-pyridinyl)amino]ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.07
465		N-(2-Chloro-6-methylphenyl)-2-[[[(1-ethyl-3-piperidinyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide	1.65

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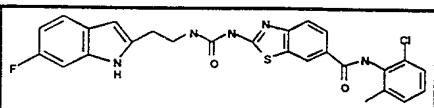
466		N-(2-Chloro-6-methylphenyl)-2-[[[[2-(6-fluoro-1H-indol-2-yl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide	2.22

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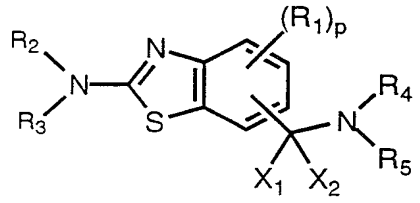
What is claimed is:

1. A benzothiazole compound of the following formula I or a salt thereof:



(I)

where

p is 0, 1, 2 or 3;

X_1 and X_2 are each hydrogen, or together form =O or =S;

each R_1 is independently selected from:

(1) hydrogen or R_6,

where R_6 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclo, or heterocycloalkyl, each of which is unsubstituted or substituted with Z_1, Z_2 and one or more groups Z_3;

(2) -OH or -OR_6;

(3) -SH or -SR_6;

(4) -$C(O)_qH$, -$C(O)_qR_6$, or -O-$C(O)_qR_6$, where q is 1 or 2;

(5) -SO_3H or -$S(O)_qR_6$;

(6) halo;

(7) cyano;

(8) nitro;

(9) -Z_4-NR_7R_8;

(10) -Z_4-$N(R_9)$-Z_5-$NR_{10}R_{11}$;

(11) -Z_4-$N(R_{12})$-Z_5-R_6;

(12) -$P(O)(OR_6)_2$;

(13) any two groups R_1 may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the carbon atoms to

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which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(14) any two groups R_1 may, together with the carbons to which they are attached, form a heterocyclo group, which group is unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_2 and R_3 are each independently:

(1) hydrogen or R_6;

(2) $-Z_4-R_6$; or

(3) $-Z_{13}-NR_7R_8$;

R_4 and R_5:

(1) are each independently hydrogen or R_6; or

(2) together with the nitrogen atom to which they are attached complete a 3- to 8-membered saturated or unsaturated heterocyclic ring which is unsubstituted or substituted with Z_1, Z_2 and Z_3, which heterocyclic ring may optionally have fused to it a benzene ring itself unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_7, R_8, R_9, R_{10}, R_{11} and R_{12}:

(1) are each independently hydrogen or R_6;

(2) R_7 and R_8 may together be alkylene or alkenylene, completing a 3- to 8-membered saturated or unsaturated ring with the nitrogen atom to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(3) any two of R_9, R_{10} and R_{11} may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_{13} is:

(1) cyano;

(2) nitro;

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(3) $-NH_2$;
(4) -NHOalkyl;
(5) -OH;
(6) -NHOaryl;
(7) -NHCOOalkyl;
(8) -NHCOOaryl;
(9) $-NHSO_2$alkyl;
(10) $-NHSO_2$aryl;
(11) aryl;
(12) heteroaryl;
(13) -Oalkyl; or
(14) -Oaryl;

R_{14} is:

(1) $-NO_2$;
(2) -COOalkyl; or
(3) -COOaryl;

Z_1, Z_2 and Z_3 are each independently:

(1) hydrogen or Z_6, where Z_6 is (i) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, alkylaryl, cycloalkylaryl, heterocyclo, or heterocycloalkyl; (ii) a group (i) which is itself substituted by one or more of the same or different groups (i); or (iii) a group (i) or (ii) which is substituted by one or more of the following groups (2) to (16) of the definition of Z_1, Z_2 and Z_3;
(2) -OH or $-OZ_6$;
(3) -SH or $-SZ_6$;
(4) $-C(O)_qH$, $-C(O)_qZ_6$, or $-O-C(O)_qZ_6$;
(5) $-SO_3H$ or $-S(O)_qZ_6$;
(6) halo;
(7) cyano;
(8) nitro;

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(9) $-Z_4-NZ_7Z_8$;

(10) $-Z_4-N(Z_9)-Z_5-NZ_7Z_8$;

(11) $-Z_4-N(Z_{10})-Z_5-Z_6$;

(12) $-Z_4-N(Z_{10})-Z_5-H$;

(13) oxo;

(14) $-O-C(O)-Z_6$;

(15) any two of Z_1, Z_2, and Z_3 may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached; or

(16) any two of Z_1, Z_2, and Z_3 may together be $-O-(CH_2)_q-O-$;

Z_4 and Z_5 are each independently:

(1) a single bond;

(2) $-Z_{11}-S(O)_q-Z_{12}-$;

(3) $-Z_{11}-C(O)-Z_{12}-$;

(4) $-Z_{11}-C(S)-Z_{12}-$;

(5) $-Z_{11}-O-Z_{12}-$;

(6) $-Z_{11}-S-Z_{12}-$;

(7) $-Z_{11}-O-C(O)-Z_{12}-$; or

(8) $-Z_{11}-C(O)-O-Z_{12}-$;

Z_7, Z_8, Z_9 and Z_{10}:

(1) are each independently hydrogen or Z_6;

(2) Z_7 and Z_8, or Z_6 and Z_{10}, may together be alkylene or alkenylene, completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(3) Z_7 or Z_8, together with Z_9, may be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3;

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Z_{11} and Z_{12} are each independently:

(1) a single bond;

(2) alkylene;

(3) alkenylene; or

(4) alkynylene;

Z_{13} is:

(1) a single bond;

(2) $-Z_{11}-S(O)_q-Z_{12}-$;

(3) $-Z_{11}-C(O)-Z_{12}-$;

(4) $-Z_{11}-C(S)-Z_{12}-$;

(5) $-Z_{11}-O-Z_{12}-$;

(6) $-Z_{11}-S-Z_{12}-$;

(7) $-Z_{11}-O-C(O)-Z_{12}-$;

(8) $-Z_{11}-C(O)-O-Z_{12}-$;

(9) $-C(NR_{13})-$;

(10) $-C(CHR_{14})-$; or

(11) $-C(C(R_{14})_2)-$.

2. A compound of claim 1, wherein p is 0 or 1, and each R_1 is independently selected from hydrogen, halo, alkyl or alkoxy.

3. A compound of claim 1, wherein R_2 is hydrogen.

4. A compound of claim 1, wherein R_3 is hydrogen, alkyl, $-Z_4-R_6$ or $-Z_{13}-NR_7R_8$.

5. A compound of claim 1, wherein R_4 is hydrogen.

6. A compound of claim 1, wherein R_5 is an aryl group which is substituted with Z_1, Z_2 and one or more groups Z_3.

7. A compound of claim 1, wherein X_1 and X_2 together form =O or =S.

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9. A method for the treatment of a protein tyrosine kinase-associated disorder, comprising the step of administering to a subject in need thereof an amount effective therefor of at least one compound of claim 1.

10. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is transplant rejection.

11. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is rheumatoid arthritis.

12. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is multiple sclerosis.

13. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is inflammatory bowel disease.

14. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is lupus.

15. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is graft vs. host disease.

16. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is a T-cell mediated hypersensitivity disease.

17. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is psoriasis.

18. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is Hashimoto's thyroiditis.

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19. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is Guillain-Barre syndrome.

20. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is a cancer where a Src-family kinase is activated or overexpressed or where Src-family kinase activity facilitates tumor growth or survival.

21. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is contact dermatitis.

22. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is an allergic disease.

23. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is asthma.

24. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is ischemic or reperfusion injury.

25. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is atopic dermatitis.

26. The method of claim 9, wherein said protein tyrosine kinase-associated disorder is allergic rhinitis.

27. The method of claim 9, wherein said protein tyrosine kinase is Lck.

28. The method of claim 9, wherein said protein tyrosine kinase is Fyn.

29. The method of claim 9, wherein said protein tyrosine kinase is Lyn.

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30. The method of claim 9, wherein said protein tyrosine kinase is Hck.

31. The method of claim 9, wherein said protein tyrosine kinase is Fgr.

32. The method of claim 9, wherein said protein tyrosine kinase is Src.

33. The method of claim 9, wherein said compound of the formula I or salt thereof is administered, simultaneously or sequentially, with an antiinflammatory, antiproliferative, chemotherapeutic agent, immunosuppressant or PTK inhibitor other than a compound of the formula I or salt thereof.

34. The method of claim 33, wherein said compound of the formula I or salt thereof is administered with one or more of: another PTK inhibitor; cyclosporin A; CTLA4-Ig; antibodies selected from anti-ICAM-3, anti-IL-2 receptor (Anti-Tac), anti-CD45RB, anti-CD2, anti-CD3 (OKT-3), anti-CD4, anti-CD80, anti-CD86, and monoclonal antibody OKT3; agents blocking the interaction between CD40 and gp39; fusion proteins constructed from CD40 and gp39; inhibitors of NF-kappa B function; non-steroidal antiinflammatory drugs (NSAIDs); steroids; gold compounds; antiproliferative agents; FK506 (tacrolimus, Prograf); mycophenolate mofetil; cytotoxic drugs; TNF-α inhibitors; anti-TNF antibodies or soluble TNF receptor; and rapamycin (sirolimus or Rapamune) or derivatives thereof.

35. A method for the treatment of a T cell mediated disorder, comprising the step of administering to a subject in need thereof an amount effective therefor of at least one compound of claim 1.

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36. The method of claim 35, wherein T cell activation is inhibited.

37. A pharmaceutical composition for the treatment of a protein kinase-associated disorder, comprising a pharmaceutically acceptable vehicle or diluent and at least one compound of claim 1.

38. A compound of claim 1, wherein:

Z_{13} is:

(1) a single bond;

(2) $-Z_{11}-S(O)_q-Z_{12}-$;

(3) $-Z_{11}-C(O)-Z_{12}-$;

(4) $-Z_{11}-C(S)-Z_{12}-$;

(5) $-Z_{11}-O-Z_{12}-$;

(6) $-Z_{11}-S-Z_{12}-$;

(7) $-Z_{11}-O-C(O)-Z_{12}-$; or

(8) $-Z_{11}-C(O)-O-Z_{12}-$.

39. A compound of claim 1, wherein:

Z_{13} is:

$-C(NR_{13})-$.

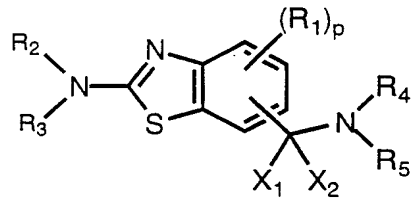
40. A compound of claim 1, wherein:

Z_{13} is:

$-C(CHR_{14})-$; or

$-C(C(R_{14})_2)-$.

41. A benzothiazole compound of the following formula I or a salt thereof:



(I)

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where

p is 0, 1, 2 or 3;

X_1 and X_2 are each hydrogen, or together form =O or =S;

each R_1 is independently selected from:

(1) hydrogen or R_6,
where R_6 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclo, or heterocycloalkyl, each of which is unsubstituted or substituted with Z_1, Z_2 and one or more groups Z_3;

(2) -OH or -OR_6;

(3) -SH or -SR_6;

(4) -$C(O)_qH$, -$C(O)_qR_6$, or -O-$C(O)_qR_6$, where q is 1 or 2;

(5) -SO_3H or -$S(O)_qR_6$;

(6) halo;

(7) cyano;

(8) nitro;

(9) -Z_4-NR_7R_8;

(10) -Z_4-$N(R_9)$-Z_5-$NR_{10}R_{11}$;

(11) -Z_4-$N(R_{12})$-Z_5-R_6;

(12) -$P(O)(OR_6)_2$;

(13) any two groups R_1 may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the carbon atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(14) any two groups R_1 may, together with the carbons to which they are attached, form a heterocyclo group, which group is unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_2 and R_3 are each independently:

(1) hydrogen or R_6;

(2) -Z_4-R_6; or

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(3) $-Z_{13}-NR_7R_8$;

R_4 and R_5:

(1) are each independently hydrogen or R_6; or

(2) together with the nitrogen atom to which they are attached complete a 3- to 8-membered saturated or unsaturated heterocyclic ring which is unsubstituted or substituted with Z_1, Z_2 and Z_3, which heterocyclic ring may optionally have fused to it a benzene ring itself unsubstituted or substituted with Z_1, Z_2 and Z_3;

R_7, R_8, R_9, R_{10}, R_{11} and R_{12}:

(1) are each independently hydrogen or R_6;

(2) R_7 and R_8 may together be alkylene or alkenylene, completing a 3- to 8-membered saturated or unsaturated ring with the nitrogen atom to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or

(3) any two of R_9, R_{10} and R_{11} may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3;

Z_1, Z_2 and Z_3 are each independently:

(1) hydrogen or Z_6, where Z_6 is (i) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, alkylaryl, cycloalkylaryl, heterocyclo, or heterocycloalkyl; (ii) a group (i) which is itself substituted by one or more of the same or different groups (i); or (iii) a group (i) or (ii) which is substituted by one or more of the following groups (2) to (16) of the definition of Z_1, Z_2 and Z_3;

(2) -OH or $-OZ_6$;

(3) -SH or $-SZ_6$;

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(4) $-C(O)_qH$, $-C(O)_qZ_6$, or $-O-C(O)_qZ_6$;
(5) $-SO_3H$ or $-S(O)_qZ_6$;
(6) halo;
(7) cyano;
(8) nitro;
(9) $-Z_4-NZ_7Z_8$;
(10) $-Z_4-N(Z_9)-Z_5-NZ_7Z_8$;
(11) $-Z_4-N(Z_{10})-Z_5-Z_6$;
(12) $-Z_4-N(Z_{10})-Z_5-H$;
(13) oxo;
(14) $-O-C(O)-Z_6$;
(15) any two of Z_1, Z_2, and Z_3 may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached; or
(16) any two of Z_1, Z_2, and Z_3 may together be $-O-(CH_2)_q-O-$;

Z_4 and Z_5 are each independently:

(1) a single bond;
(2) $-Z_{11}-S(O)_q-Z_{12}-$;
(3) $-Z_{11}-C(O)-Z_{12}-$;
(4) $-Z_{11}-C(S)-Z_{12}-$;
(5) $-Z_{11}-O-Z_{12}-$;
(6) $-Z_{11}-S-Z_{12}-$;
(7) $-Z_{11}-O-C(O)-Z_{12}-$; or
(8) $-Z_{11}-C(O)-O-Z_{12}-$;

Z_7, Z_8, Z_9 and Z_{10}:

(1) are each independently hydrogen or Z_6;
(2) Z_7 and Z_8, or Z_6 and Z_{10}, may together be alkylene or alkenylene, completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; or
(3) Z_7 or Z_8, together with Z_9, may be alkylene or alkenylene completing a 3- to 8-membered saturated or

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unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with Z_1, Z_2 and Z_3; and

Z_{11} and Z_{12} are each independently:

(1) a single bond;

(2) alkylene;

(3) alkenylene; or

(4) alkynylene;

Z_{13} is:

(1) a single bond;

(2) $-Z_{11}-S(O)_q-Z_{12}-$;

(3) $-Z_{11}-C(O)-Z_{12}-$;

(4) $-Z_{11}-C(S)-Z_{12}-$;

(5) $-Z_{11}-O-Z_{12}-$;

(6) $-Z_{11}-S-Z_{12}-$;

(7) $-Z_{11}-O-C(O)-Z_{12}-$; or

(8) $-Z_{11}-C(O)-O-Z_{12}-$.

42. A compound of claim 41, which compound of the formula I or salt thereof is selected from the group consisting of:

[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

2-(Acetylamino)-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-(Benzoylamino)-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxobutyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[Bis(1-methylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

[6-Bromo-4-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[4-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-Bromo-7-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[7-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-Bromo-5-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[5-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-[[[Phenylamino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(Phenylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[Ethylamino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Butylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopropylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[[(3,3-Dimethylcyclohexyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methylcyclohexyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(Cyclohexylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Naphthalenylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Morpholinyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(2-Pyridinyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1,3,3-Tetramethylbutyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,5-Dimethylhexyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopentylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(3-Methylphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Chlorophenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Methoxyphenyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propynylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propenylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[4-(1,1-Dimethylethyl)cyclohexyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Propylbutyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,3-Dimethylpentyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[3-(Methylthio)propyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(2-Thienyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(2,6-Dimethoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[[1-(Hydroxymethyl)-2-phenylethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1-Adamantylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Fluorophenyl)-1,1-dimethylethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(2-Pyridinyloxy)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Methyl-1-phenylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[[1-(4-Methylphenyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Methylheptyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Cyclohexylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(5,6,7,8-Tetrahydro-1-naphthalenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-5-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Pyridinylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Methyl-2-pyridinyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methyl-2-pyridinyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Chloro-5-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,6-Dichlorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[([1,1'-Biphenyl]-2-ylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Benzoylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,4,6-Trimethylphenyl)-2-[[[(2,4,6-trimethylphenyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[[2-Methyl-6-(1-methylethyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3,5-Difluorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[(3-Methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Cyanophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Chlorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

4-[[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]benzoic acid, ethyl ester;

2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3,4-Dimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2,6-Bis(1-Methylethyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Propylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Bromo-2,4,6-trimethylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Morpholinyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Bromo-2-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,6-Dimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Bromo-5-methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Methoxy-6-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dimethyl-1H-indol-5-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[[3-(1,3,4-Oxadiazol-2-yl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Chloro-6-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[3-(Methylthio)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methoxy-2-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(4-Methoxycyclohexyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2,2-Dimethyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Thienylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclopropylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclobutylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclopentylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(3-Cyclopentyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Cyclopenten-1-ylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclohexylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-2-phenylpropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Methyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-3-phenoxypropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-3-phenylpropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[3-(2-Methoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(2,3,4-Trimethoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1,4-Dioxopentyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Naphthalenylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Chloro-6-fluorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Methylphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(3-Methoxyphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(4-Chlorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-4-pentynyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

5-Oxo-5-[[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]pentanoic acid, methyl ester;

2-[(1-Oxohexyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxoheptyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

2-[[1-Oxo-4-(2-thienyl)butyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(3-Thienylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(4-Nitrophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3,5-Bis(trifluoromethyl)phenyl]acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[2-[4-(2-Methypropyl)phenyl]-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[(3-Cyclohexen-1-yl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(3-Methoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2,3,6-Trichlorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-yl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[2-(Phenylmethoxy)phenyl]acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(3,5-Dimethoxyphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(1,3-Benzodioxol-5-yl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Tetrahydro-2-furanyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[2-(Acetylamino)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[2-(Acetylamino)-1-oxohexyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclopropylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

N,N-Dimethyl-N'-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]butanediamide;

2-[(1-Adamantylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(4-Methylcyclohexyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(3-Methoxy-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

[6-[[(2,3-Dihydro-1H-inden-5-yl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[(2-Naphthylenylamino)carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

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[6-[[(3-Hydroxy-2-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Fluoro-5-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(4-Bromo-2-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(3-Bromo-2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[2,6-Dimethyl-3-(1-methylethyl)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Bromo-4,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Methyl-6-quinolinyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(4-Methoxy-2-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(6-Methyl-5-quinolinyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[2-(2-Hydroxyethyl)-6-methylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2,6-Dimethyl-3-nitrophenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Bromo-3,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Acetyl-6-hydroxyphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[4-[[(1,1-Dimethylethoxy)carbonyl]amino]-2,3,5,6-tetramethylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

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[6-[[(4-Bromo-2,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[3-Acetylamino]-4,6-dimethylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2,6-Dimethoxyphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Methyl-1-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

3-[[[2-[[(1,1-Dimethylethoxy)carbonyl]amino]-6-benzothiazolyl]carbonyl]amino]-4-methyl-2-thiophenecarboxylic acid, methyl ester;

[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, methyl ester;

2-[[(Acetylamino)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dichlorophenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(4-Bromo-2,6-dimethylphenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(4-Carbomethoxy-2,6-Dimethylphenyl)-2-[[[1,1-dimethylethoxy]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(4-Hydroxymethyl-2,6-Dimethylphenyl)-2-[[[1,1-dimethylethoxy]carbonyl]amino]-6-benzothiazolecarboxamide;

[4-Methyl-6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-4-methyl-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

4-Methoxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-4-methoxy-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

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2-[[(Methylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[Methylamino]carbonyl]amino]-4-methoxy-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

5-Methoxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-N-(4-N,N-dimethylamino-2,3,5,6-tetramethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

5-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

7-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-5-hydroxy-N-[2,4,6-trimethylphenyl]-6-benzothiazolecarboxamide;

5-*tert*-Butoxycarbonyloxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopropylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopentylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(ethynyl)cyclohexyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methyl-cyclohexyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

QA207a

2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propynylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propenylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopropylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopentylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(ethynyl)cyclohexyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

QA207a

2-[[[(4-Methyl-cyclohexyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propynylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propenylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dimethyl-1H-indol-5-yl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

QA207a

2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(1-methoxycarbonyl)cyclopropyl]amino]carbonyl]amino-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

[6-[[[(2,6-Dimethyl-4-phenyl)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[(2,6-Dimethyl-4-(2-N,N-dimethylethoxy)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[(2,6-Dimethyl-4-(2-morpholinoethoxy)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-[(Cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Methyl-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[(2,2-Dichloro-1-methyl-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Hydroxy-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(cyclobutylcarbonyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(cyclopentylcarbonyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(cyclohexylacetyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(methoxyacetyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-2-phenylpropyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-2-methylpropyl)amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-3-phenylpropyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[3-(2-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[1-oxo-3-(2,3,4-trimethoxyphenyl)propyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(1,4-dioxopentyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(2,2-dimethyl-1-oxobutyl)amino]-6-benzothiazolecarboxamide;

2-[[(2-Chloro-6-fluorophenyl)acetyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(2-methylphenyl)acetyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(3-methoxyphenyl)acetyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(4-chlorophenyl)acetyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(1-oxo-4-pentynyl)amino]-6-benzothiazolecarboxamide;

5-[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]-5-oxopentanoic acid methyl ester;

N-(2-Chloro-6-methylphenyl)-2-[(1-oxohexyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[3-(3-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-yl)acetyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(1,3-Benzodioxol-5-yl)-1-oxopropyl;]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(3,5-dimethoxyphenyl)acetyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(cyclopropylacetyl)amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[(1-methylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[2-(trimethylsilyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[1-(4-methoxyphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[(2-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[1-(4-methylphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[1-(4-chlorophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

[1-[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropyl]carbamic acid 1,1-dimethylethyl ester;

(1S-trans)-N-(2-Chloro-6-methylphenyl)-2-[[[2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

(1S-cis)-N-(2-Chloro-6-methylphenyl)-2-[[[2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(1-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(2-formylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropanecarboxylic acid ethyl ester;

2-[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]-1-methylcyclopropanecarboxylic acid methyl ester;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[[2-(phenylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

N-[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]-2-quinolinecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(2-pyridinylcarbonyl)amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[(2-pyridinylcarbonyl)amino]-6-benzothiazolecarboxamide, 1-oxide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[(dimethylamino)methyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(1-methyl-1H-pyrrol-2-yl)acetyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[5-(dimethylamino)-1-oxopentyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[4-(dimethylamino)-1-oxobutyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(1-pyrrolidinylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(1-piperidinylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(dimethylamino)acetyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[3-(2-methyl-4-nitro-1H-imidazol-1-yl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide;

2-[(Cyclobutylcarbonyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclopentylcarbonyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclohexylacetyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

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N-(2,6-Dimethylphenyl)-2-[(1-oxo-2-phenylpropyl)amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[(2-methyl-1-oxopropyl)amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[(1-oxo-3-phenylpropyl)amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[3-(2-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[3-(2,3,4-trimethoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[(1,4-dioxopentyl)amino]-6-benzothiazolecarboxamide;

2-[(2,2-Dimethyl-1-oxobutyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[(methoxyacetyl)amino]-6-benzothiazolecarboxamide;

N,N-Dimethyl-N'-[6-[[(2,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]butanediamide;

N-(2,6-Dimethylphenyl)-2-[[(1-methylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[(2-Chloro-6-fluorophenyl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[(2-methylphenyl)acetyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[(3-methoxyphenyl)acetyl]amino]-6-benzothiazolecarboxamide;

2-[[(4-Chlorophenyl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[(1-oxo-4-pentynyl)amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[(1-oxohexyl)amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[3-(3-methoxyphenyl)-1-oxopropyl]amino]-6-benzothiazolecarboxamide;

QA207a

2-[[3-(1,3-Benzodioxol-5-yl)-1-oxopropyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-yl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(3,5-Dimethoxyphenyl)acetyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclopropylacetyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[[2-(phenylmethyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[[2-(trimethylsilyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[(Cyclopropylcarbonyl)amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[(2-methylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2,6-Dimethylphenyl)-2-[[(2-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[[1-(4-methylphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[1-(4-Chlorophenyl)cyclopropyl]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

[1-[[[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropyl]carbamic acid 1,1-dimethylethyl ester;

(1S-cis)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[[1-(4-methoxyphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

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N-(2,6-Dimethylphenyl)-2-[[(1-phenylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dimethylphenyl)-2-[[(2-formylcyclopropyl)carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropanecarboxylic acid ethyl ester;

2-[[(2-Cyanocyclopropyl)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]-1-methylcyclopropanecarboxylic acid methyl ester;

(1S-trans)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,4,6-Trimethylphenyl)-2-[[[2-(trimethylsilyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[(2-Methylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

trans-2-[[(2-Phenylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropanecarboxylic acid ethyl ester;

[1-[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]cyclopropyl]carbamic acid 1,1-dimethylethyl ester;

(1S-trans)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(1S-cis)-2-[[[2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1-Phenylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

QA207a

2-[[(2-Formylcyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Cyanocyclopropyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]-1-methylcyclopropanecarboxylic acid methyl ester;

2-[[[2-(Phenylmethyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[1-(4-Methylphenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[1-(4-Chlorophenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[1-(4-Methoxyphenyl)cyclopropyl]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-piperidinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2-chlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2-fluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(2-phenoxyethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[(Benzo[b]thiophen-3-ylmethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

(R)-N-(2-Chloro-6-methylphenyl)-2-[[[(2-hydroxy-1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(dimethylamino)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(S)-N-(2-Chloro-6-methylphenyl)-2-[[[(2-hydroxy-1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[[[(4-nitrophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-pyrrolidinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(2- N-(2-Chloro-6-methylphenyl)-2-[[[(3-pyridinylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(4-pyridinylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3-chlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,3-dichlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3,4-difluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,6-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2-ethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,3-dihydro-1,4-benzodioxin-2-yl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(3-methoxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(4-methoxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(5-methyl-2-furanyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(hydroxymethyl)-2-phenylethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(phenylamino)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(2-thienylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1H-indol-3-yl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[[(4-Aminophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(diphenylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(1R-exo)-2-[[(Bicyclo[2.2.1]heptan-2-ylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(4-chlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-chlorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-methylphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-methylphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(4-fluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-fluorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(2-furanylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-methoxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(S)-N-(2-Chloro-6-methylphenyl)-2-[[[(1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

α-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]benzeneacetic acid ethyl ester;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(4-methylphenyl)-1-phenylethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(R)-N-(2-Chloro-6-methylphenyl)-2-[[[(1-phenylpropyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(4-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-nitrophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(4-chlorophenyl)phenylmethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(phenylthio)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

2-[[[[(2-Bromophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(3-fluorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(trifluoromethyl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[[(3-Bromophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Chloro-2-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Amino-2-oxo-1-phenylethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(1H-imidazol-1-yl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,4-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3-chloro-4-methylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[[(3-Chloro-4-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(2-Chloro-6-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(2-Chloro-4-fluorophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3,5-difluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,5-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[[[(3,5-dimethylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3,4-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3,5-dimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(1-methylethyl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(2-chlorophenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(1-methyl-1-phenylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,5-dichlorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,4-dimethylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3,4,5-trimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,4,6-trimethoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

2-[[[[(4-Bromophenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

[1R-(endo,endo)]-3-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]bicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester;

[1S-(exo,exo)]-3-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]bicyclo[2.2.1]heptane-2-carboxylic acid ethyl ester;

[1R-(exo,exo)]-3-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]bicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester;

[1R-(endo,endo)]-N-(2-Chloro-6-methylphenyl)-2-[[[[3-(hydroxymethyl)bicyclo[2.2.1]hept-5-en-2-yl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

[1S-(endo,endo)]-N-(2-Chloro-6-methylphenyl)-2-[[[[3-(hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

[1R-(exo,exo)]-N-(2-Chloro-6-methylphenyl)-2-[[[[3-(hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(3-fluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2-methoxyphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(exo,exo)-2-[[[[3-(Aminocarbonyl)bicyclo[2.2.1]hept-5-en-2-yl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[[[[3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(phenylmethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(endo,endo)-2-[[[[3-(Aminocarbonyl)bicyclo[2.2.1]hept-5-en-2-yl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(4-hydroxyphenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,6-difluorophenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[(2,3-dimethylphenyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(dimethylamino)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1,1-dimethyl-2-(dimethylamino)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(2-methyl-1-piperidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(4-morpholinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(diethylamino)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(4-methyl-1-piperazinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1-piperazinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(4-morpholinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(2,2,6,6-tetramethyl-4-piperidinyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(R)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

(S)-N-(2-Chloro-6-methylphenyl)-2-[[[[1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(1-piperidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(1-pyrrolidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(2-pyridinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[1-(3-pyridinyl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

4-[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]-1-piperidinecarboxylic acid ethyl ester;

(S)-2-[[[[1-(4-Bromophenyl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

(1S-cis)-2-[[[[2-(Aminocarbonyl)cyclohexyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[3-(1H-Azepin-1-yl)propyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2,2-dimethyl-3-(dimethylamino)propyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(3-pyrrolidinylamino)carbonyl]amino]-6-benzothiazolecarboxamide;

4-[[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]methyl]benzoic acid;

N-(2-Chloro-6-methylphenyl)-2-[[(3-pyridinylamino)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(4-pyridinylamino)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(1H-pyrrol-3-yl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(2-pyridinylamino)carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[(2-pyrimidinylamino)carbonyl]amino]-6-benzothiazolecarboxamide;

4-[[[[[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]methyl]benzoic acid methyl ester;

N-(2-Chloro-6-methylphenyl)-2-[[[[(1-ethyl-2-pyrrolidinyl)methyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

QA207a

N-(2-Chloro-6-methylphenyl)-2-[[[[2-[(5-nitro-2-pyridinyl)amino]ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[(1-ethyl-3-piperidinyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2-Chloro-6-methylphenyl)-2-[[[[2-(6-fluoro-1H-indol-2-yl)ethyl]amino]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[4-(1,1-dimethylethyl)phenyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-ethoxyphenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-fluorophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[4-(1-methylethyl)phenyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-[4-(trifluoromethyl)phenyl]cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-nitrophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(4-cyanophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-2-[[(2-[1,1'-Biphenyl]-4-ylcyclopropyl)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

trans-2-[[[2-(1,3-Benzodioxol-4-yl)cyclopropyl]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(3-chlorophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide;

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(3-cyanophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide; and

QA207a

trans-N-(2-Chloro-6-methylphenyl)-2-[[[2-(3-nitrophenyl)cyclopropyl]carbonyl]amino]-6-benzothiazolecarboxamide.

43. A compound of claim 41, which compound of the formula I or salt thereof is selected from the group consisting of:

[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

2-(Acetylamino)-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-(Benzoylamino)-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxobutyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[Bis(1-methylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

[6-Bromo-4-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[4-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-Bromo-7-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[7-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-Bromo-5-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[5-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

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2-[[[Phenylamino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(Phenylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[Ethylamino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Butylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopropylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[[(3,3-Dimethylcyclohexyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methylcyclohexyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(Cyclohexylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Naphthalenylmethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Morpholinyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(2-Pyridinyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1,3,3-Tetramethylbutyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

QA207a

2-[[[(1,5-Dimethylhexyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopentylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(3-Methylphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Chlorophenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Methoxyphenyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propynylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propenylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[4-(1,1-Dimethylethyl)cyclohexyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Propylbutyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,3-Dimethylpentyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[3-(Methylthio)propyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(2-Thienyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

QA207a

2-[[[[(2,6-Dimethoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[[1-(Hydroxymethyl)-2-phenylethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1-Adamantylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Fluorophenyl)-1,1-dimethylethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(2-Pyridinyloxy)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Methyl-1-phenylethyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[[1-(4-Methylphenyl)ethyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1-Methylheptyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Cyclohexylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(5,6,7,8-Tetrahydro-1-naphthalenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-5-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Pyridinylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Methyl-2-pyridinyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[(4-Methyl-2-pyridinyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Chloro-5-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,6-Dichlorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[([1,1'-Biphenyl]-2-ylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Benzoylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

N-(2,4,6-Trimethylphenyl)-2-[[[(2,4,6-trimethylphenyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

2-[[[[2-Methyl-6-(1-methylethyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3,5-Difluorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Cyanophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Chlorophenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

4-[[[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]carbonyl]amino]benzoic acid, ethyl ester;

2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[(3,4-Dimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2,6-Bis(1-Methylethyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Propylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Bromo-2,4,6-trimethylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(4-Morpholinyl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Bromo-2-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,6-Dimethoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Bromo-5-methoxyphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Methoxy-6-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dimethyl-1H-indol-5-yl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[3-(1,3,4-Oxadiazol-2-yl)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2-Chloro-6-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[3-(Methylthio)phenyl]amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methoxy-2-methylphenyl)amino]carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(4-Methoxycyclohexyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2,2-Dimethyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Thienylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[(Cyclopropylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclobutylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclopentylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(3-Cyclopentyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Cyclopenten-1-ylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclohexylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-2-phenylpropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Methyl-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-3-phenoxypropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-3-phenylpropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(2-Methoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(2,3,4-Trimethoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1,4-Dioxopentyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Naphthalenylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Chloro-6-fluorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Methylphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(3-Methoxyphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[(4-Chlorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxo-4-pentynyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

5-Oxo-5-[[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]amino]pentanoic acid, methyl ester;

2-[(1-Oxohexyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(1-Oxoheptyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide

2-[[1-Oxo-4-(2-thienyl)butyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(3-Thienylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(4-Nitrophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3,5-Bis(trifluoromethyl)phenyl]acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[2-[4-(2-Methypropyl)phenyl]-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(3-Cyclohexen-1-yl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(3-Methoxyphenyl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2,3,6-Trichlorophenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-yl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[2-(Phenylmethoxy)phenyl]acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(3,5-Dimethoxyphenyl)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[3-(1,3-Benzodioxol-5-yl)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[(Tetrahydro-2-furanyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[2-(Acetylamino)-1-oxopropyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[2-(Acetylamino)-1-oxohexyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(Cyclopropylacetyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

N,N-Dimethyl-N'-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]butanediamide;

2-[(1-Adamantylcarbonyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(4-Methylcyclohexyl)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[(3-Methoxy-1-oxopropyl)amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

[6-[[(2,3-Dihydro-1H-inden-5-yl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[(2-Naphthylenylamino)carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(3-Hydroxy-2-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Fluoro-5-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Chloro-6-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2,6-Dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(4-Bromo-2-methylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(3-Bromo-2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[2,6-Dimethyl-3-(1-methylethyl)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

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[6-[[(2-Bromo-4,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Methyl-6-quinolinyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(4-Methoxy-2-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(6-Methyl-5-quinolinyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[2-(2-Hydroxyethyl)-6-methylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2,6-Dimethyl-3-nitrophenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Bromo-3,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Acetyl-6-hydroxyphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[4-[[(1,1-Dimethylethoxy)carbonyl]amino]-2,3,5,6-tetramethylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(4-Bromo-2,6-dimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[3-Acetylamino]-4,6-dimethylphenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2,6-Dimethoxyphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[(2-Methyl-1-naphthalenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

3-[[[2-[[(1,1-Dimethylethoxy)carbonyl]amino]-6-benzothiazolyl]carbonyl]amino]-4-methyl-2-thiophenecarboxylic acid, methyl ester;

[6-[[(2,4,6-Trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, methyl ester;

2-[[(Acetylamino)acetyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

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N-(2-Chloro-6-methylphenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(2,6-Dichlorophenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(4-Bromo-2,6-dimethylphenyl)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(4-Carbomethoxy-2,6-Dimethylphenyl)-2-[[[1,1-dimethylethoxy]carbonyl]amino]-6-benzothiazolecarboxamide;

N-(4-Hydroxymethyl-2,6-Dimethylphenyl)-2-[[[1,1-dimethylethoxy]carbonyl]amino]-6-benzothiazolecarboxamide;

[4-Methyl-6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-4-methyl-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

4-Methoxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-4-methoxy-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

2-[[(Methylamino)carbonyl]amino]-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[Methylamino]carbonyl]amino]-4-methoxy-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

5-Methoxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-N-(4-N,N-dimethylamino-2,3,5,6-tetramethylphenyl)-6-benzothiazolecarboxamide, trifluoroacetate (1:1);

5-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

7-Chloro-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-Amino-5-hydroxy-N-[2,4,6-trimethylphenyl]-6-benzothiazolecarboxamide;

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5-*tert*-Butoxycarbonyloxy-[6-[[(2,4,6-trimethylphenyl)amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

2-[[[(1,1-Dimethylethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopropylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopentylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(ethynyl)cyclohexyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methyl-cyclohexyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propynylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propenylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

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2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2,6-dimethylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopropylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[(Cyclopentylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(ethynyl)cyclohexyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Methyl-cyclohexyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dihydro-1H-inden-1-yl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(1H-Imidazol-4-yl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(Tetrahydro-2-furanyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[2-(5-Methoxy-1H-indol-3-yl)ethyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-2-hydroxyethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(1,1-Dimethyl-propyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

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2-[[[[(3-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(4-Methoxyphenyl)methyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propynylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[(2-Propenylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3-Phenylpropyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Hydroxymethyl)cyclopentyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[1-(Methoxymethyl)propyl]amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

(R)-2-[[[(1-Phenylethyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(2,3-Dimethyl-1H-indol-5-yl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(3,4,5-Trimethoxyphenyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[(1,3-Benzodioxol-5-ylamino)carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[[[[(1-methoxycarbonyl)cyclopropyl]amino]carbonyl]amino-N-(2,4,6-trimethylphenyl)-6-benzothiazolecarboxamide;

[6-[[[(2,6-Dimethyl-4-phenyl)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[(2,6-Dimethyl-4-(2-N,N-dimethylethoxy)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

[6-[[[(2,6-Dimethyl-4-(2-morpholinoethoxy)phenyl]amino]carbonyl]-2-benzothiazolyl]carbamic acid, 1,1-dimethylethyl ester;

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2-[(Cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[(2-Methyl-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide;

2-[(2,2-Dichloro-1-methyl-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide; and

2-[(1-Hydroxy-cyclopropylcarbonyl)amino]-N-(2-chloro-6-methylphenyl)-6-benzothiazolecarboxamide.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/23204

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/212, 233.8, 255, 269, 314, 321, 338, 367; 540/524; 544/135, 297, 368; 546/171, 198, 270.1; 548/159, 163, 164

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,317,682 A (KATSURA ET AL.) 02 March 1982 (02/03/82), see entire document, especially column 7, Preparatory Example 6.	1-7, 38-41
X	US 4,970,318 A (SCHNUR ET AL.) 13 November 1990 (13/11/90), see entire document, especially column 1, Formulas I and II.	1-7, 9, 20, 27-34, 37-41
X	US 5,036,086 A (TAGUCHI ET AL.) 30 July 1991 (30/07/91), see entire document, especially column 1.	1-5, 7, 9, 22, 23, 26, 37-41

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 31 DECEMBER 1998	Date of mailing of the international search report 23 FEB 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer LAURA L. STOCKTON Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet)(July 1992)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/23204

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

A61K 31/425, 31/44, 31/445, 31/47, 31/50, 31/505, 31/535, 31/55; C07D 277/82, 401/06, 407/06, 409/06, 413/06, 417/06, 471/04

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

514/212, 233.8, 255, 269, 314, 321, 338, 367; 540/524; 544/135, 297, 368; 546/171, 198, 270.1; 548/159, 163, 164